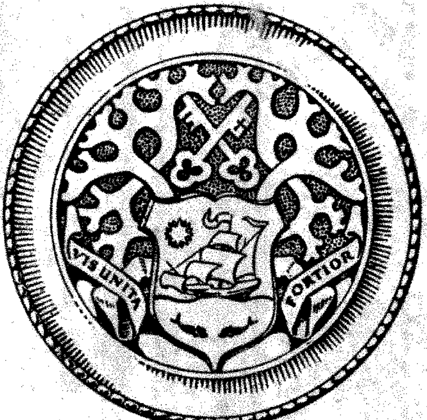
i6 CUlc - 1406246 - 5 - P25869

BRITISH JOURNAL OF UROLOGY

Official Journal of the
British Association of Urological Surgeons
(Home and Overseas)

5



LIBRARY

Volume 48 No 1

February 1976

E & S Livingstone

BRITISH JOURNAL OF UROLOGY

EDITOR
* W. KEITH YEATES

HON. TREASURER
* C. H. KINDER

ASSISTANT EDITORS
* G. D. CHISHOLM
* D. M. ESSENHIGH
* W. F. HENDRY
* W. SELBY TULLOCH

ASSISTANT EDITOR FOR AUSTRALASIA
G. F. MURNAGHAN

CONSULTING EDITORS
* DAVID BAND
* J. D. FERGUSSON

EDITORIAL COMMITTEE
Chairman D. INNES WILLIAMS*

G. H. BAINES, Birmingham
JOHN BALFOUR, Vancouver
D. R. BARNES, Cape Town
J. P. BLANDY, London
JEAN CHARBONNEAU, Montreal
C. A. C. CHARLTON, Bath
PHILIP CLARK, Leeds
B. N. COLABAWALLA, Bombay
M. H. DEVEREUX, Loughton, Essex
J. N. de KLERK, Cape Town
E. CHARLTON EDWARDS, Manchester
E. J. ENGLAND, Perth, W. Australia
H. FINE, Durban
ALBAN H. GEE, Sydney
N. O. K. GIBBON, Liverpool
JOHN GRIEVE, Dundee
A. R. HARRISON, London
D. K. KARANJAVALA, Bombay
J. A. KENNEDY, Belfast
W. K. KERR, Toronto
KENNETH J. MACKINNON, Montreal
J. W. F. MACKY, Auckland
JOHN P. MADDERN, Adelaide
J. P. MITCHELL, Bristol
*RICHARD A. MOGG, Cardiff
J. DERMOT O'FLYNN, Dublin
H. H. PEARSON, M.B.E., Canberra
J. S. PETERS, Melbourne
R. C. B. PUGH, London
P. J. M. RETIEF, Cape Town
CHARLES J. ROBSON, Toronto
L. STUART SCOTT, Glasgow
K. E. D. SHUTTLEWORTH, London
SARINDER MAN SINGH, Delhi
J. C. SMITH, Oxford
J. J. STEVENSON, London
J. H. STEYN, Aberdeen
W. BARR STIRLING, Glasgow
JOHN SWINNEY, M.C., Bunbury, W. Australia
G. C. TRESIDDER, London
P. J. P. VAN BLERK, Johannesburg
DAVID M. WALLACE, O.B.E., London
J. G. WATSON, Brisbane
R. H. WHITAKER, Cambridge
*J. L. WILLIAMS, Sheffield
J. F. R. WITHYCOMBE, Cambridge

* Members of Executive Committee

ST PETER'S MEDAL AWARDED TO

J. B. MACALPINE, 1949
R. OGIER WARD, 1951
TERENCE J. MILLIN, 1951
A. CLIFFORD MORSON, 1954
LESLIE N. PYRAH, 1959
CUTHBERT E. DUKES, 1960
DAVID BAND 1962
SIR ERIC RICHES, 1964

THE BRITISH ASSOCIATION OF UROLOGICAL SURGEONS

ARTHUR H. JACOBS, 1965
D. INNES WILLIAMS, 1967
H. HAMILTON STEWART, 1968
JOHN SWINNEY, 1969
SIR MICHAEL WOODRUFF, 1970
D. S. POOLE-WILSON, 1971
DAVID M. WALLACE, 1973
A. W. BADENOCH, 1974
HOWARD G. HANLEY, 1975

P25869

E. & S. Livingstone
Edinburgh and London
February 1976

BRITISH JOURNAL OF UROLOGY

EDITOR
* W. KEITH YEATES

HON. TREASURER
* C. H. KINDER

ASSISTANT EDITORS
* G. D. CHISHOLM
* D. M. ESSENHIGH
* W. F. HENDRY
* W. SELBY TULLOCH

ASSISTANT EDITOR FOR AUSTRALASIA
G. F. MURNAGHAN

CONSULTING EDITORS
* DAVID BAND
* J. D. FERGUSSON

EDITORIAL COMMITTEE
Chairman D. INNES WILLIAMS*

M. HANDLEY ASHKEN, Norwich
G. H. BAINES, Birmingham
JOHN BALFOUR, Vancouver
D. R. BARNES, Cape Town
*J. P. BLANDY, London
JEAN CHARBONNEAU, Montreal
C. A. C. CHARLTON, Bath
PHILIP CLARK, Leeds
B. N. COLABAWALLA, Bombay
M. H. DEVEREUX, Loughton, Essex
J. N. de KLERK, Cape Town
E. CHARLTON EDWARDS, Manchester
E. J. ENGLAND, Perth, W. Australia
H. FINE, Durban
ALBAN H. GEE, Sydney
N. O. K. GIBBON, Liverpool
JOHN GRIEVE, Dundee
A. R. HARRISON, London
D. K. KARANJAVALA, Bombay
J. A. KENNEDY, Belfast
W. K. KERR, Toronto
KENNETH J. MACKINNON, Montreal
J. W. F. MACKY, Auckland
JOHN P. MADDERN, Adelaide
*J. P. MITCHELL, Bristol
*RICHARD A. MOGG, Cardiff
J. DERMOT O'FLYNN, Dublin
H. H. PEARSON, M.B.E., Canberra
J. S. PETERS, Melbourne
R. C. B. PUGH, London
P. J. M. RETIEF, Cape Town
CHARLES J. ROBSON, Toronto
L. STUART SCOTT, Glasgow
K. E. D. SHUTTLEWORTH, London
SARINDER MAN SINGH, Delhi
J. C. SMITH, Oxford
J. J. STEVENSON, London
*J. H. STEYN, Aberdeen
W. BARR STIRLING, Glasgow
JOHN SWINNEY, M.C., Bunbury, W. Australia
G. C. TRESIDDER, London
P. J. P. VAN BLERK, Johannesburg
DAVID M. WALLACE, O.B.E., London
J. G. WATSON, Brisbane
R. H. WHITAKER, Cambridge
*J. L. WILLIAMS, Sheffield
J. F. R. WITHYCOMBE, Cambridge
P. H. L. WORTH, London

* Members of Executive Committee

ST PETER'S MEDAL AWARDED TO

J. B. MACALPINE, 1949
R. OGIER WARD, 1951
TERENCE J. MILLIN, 1951
A. CLIFFORD MORSON, 1954
LESLIE N. PYRAH, 1959
CUTHBERT E. DUKES, 1960
DAVID BAND, 1962
SIR ERIC RICHES, 1964
ARTHUR H. JACOBS, 1965

THE BRITISH ASSOCIATION OF UROLOGICAL SURGEONS

D. INNES WILLIAMS, 1967
H. HAMILTON STEWART, 1968
JOHN SWINNEY, 1969
SIR MICHAEL WOODRUFF, 1970
D. S. POOLE-WILSON, 1971
DAVID M. WALLACE, 1973
A. W. BADENOCH, 1974
HOWARD G. HANLEY, 1975

VOLUME 48
(1976)
E. & S. LIVINGSTONE

All rights reserved. No part of this publication may be reproduced, stored in a retrieval system, or transmitted in any form or by any means, electronic, mechanical, photocopying, recording or otherwise, without the prior permission of the copyright owner

©

E. & S. LIVINGSTONE, 1976

CONTENTS

ORIGINAL ARTICLES— PAGE

Uric Acid Disorders in Patients with Calcium Stones. By A. Hodgkinson 1
Urinary Citrate Excretion in Stone-formers and Normal Controls. By S. G. Welshman and M. G. McGeown 7
The Elastic Component of Normal and Dilated Ureters in Children: Chemical and Histochemical Characterisation. By F. Pagano, G. Passerini, R. Cortivo, D. Daga-Gordini and G. Abatangelo 13
Experience with the Ileal Ureter. By Hessein A. Amin 19
Endometriosis Mimicking Ureterolithiasis. By Y. M. Traub, J. Fischelovitch, A. Neri and E. Lubin 27
Re-implantation of the Ureter. By Philip Clark and R. U. Hosmane 31
First Report on the Standardisation of Terminology of Lower Urinary Tract Function. Produced by the International Continence Society, February, 1975 39
Innervation of the Muscle of the Bladder in the Rat. By A. D. Hoyes, R. Bourne and B. G. H. Martin 43
Single Dose Intravesical Thiotepa as an Adjuvant to Cystodiathermy in the Treatment of Transitional Cell Bladder Carcinoma. By K. G. Burnand, P. J. R. Boyd, M. E. Mayo, K. E. D. Shuttleworth and R. W. Lloyd-Davies 55
Studies on the Chemical Nature of Urinary Chemiluminescence. By G. Alan Rose 61
The Effect of Bromocriptine in Patients with Benign Prostatic Hypertrophy. By D. J. Farrar and J. S. Pryor 73
A Study of Concentrations of Trimethoprim-Sulphamethoxazole in the Human Prostate Gland. By N. F. Dabhoiwala, A. Bye and M. Claridge 77
Badenoch's Pull-through Operation for Urethral Stricture. By G. H. Tilak, H. C. Dhayagude and S. S. Joshi 83
Diphosphonate Therapy in Nephrocalcinosis. By D. A. McCredie, H. R. Powell and E. Rotenberg 93
The Surgical Management of Tuberculous Lower Ureteric Stricture. By P. J. O'Boyle, E. M. Galli and J. G. Gow 101
Traumatic Avulsion of the Ureter with Obstruction, Pseudocyst Formation and Hypertension. By B. F. Ribeiro and J. K. M. Quartey 107
Influence of Vesico-ureteral Reflux on the Response to Treatment of Urinary Tract Infections in Female Children. By William R. Fair and Duncan E. Govan 111
Percutaneous Suprapubic Cystostomy after Spinal Cord Injury. By J. B. Cook and P. H. Smith . 119
Asymptomatic Phaeochromocytoma of the Bladder Co-existing with Carcinoma. By C. H. Leong, K. K. Wong and D. Saw 123
Male Epispadias: Surgical Repairs of Urethropenile Deformity. By Emil A. Tanagho 127
An Unusual Case of Right and Left Testicular Arteries Arching over the Left Renal Vein. By Hilel Nathan, Philip V. Tobias and Michael D. Wellsted 135
A.I.D.—A Review of 200 Cases. By Robert Newill 139
Some Observations on the Medulla of the Kidney. By H. Fine and E. N. Keen 161
Crossed Renal Ectopia with Colic: a Clinical Clue to Embryogenesis. By D. G. Romans, M. A. S. Jewett and C. J. Robson 171
Hydronephrosis and Polycythaemia. By A. Sriman Narayana, F. Gallagher, D. G. Kelly and F. A. Duff 175
A Simple Method for Studying the Formation of Calcium Oxalate. By D. June Sutor 177
Circumcaval Ureter: A Report of Four Cases in Children with a Review of the Literature and a New Classification. By M. M. Kenawi and D. Innes Williams 183
Abnormalities of Detrusor and Sphincter Function in Multiple Sclerosis. By Jens T. Andersen and William E. Bradley 193
A Case of Behçet's Disease involving the Bladder. By G. F. Carswell 199
Preliminary Communication: Cryosurgery for Prostatic Obstruction using Liquid Nitrous Oxide. By B. M. Wright 203
Latent Carcinoma of the Prostate: the Probability of Identifying Small Lesions in Routine Histology. By G. S. Delides, G. Baltopoulos and N. X. Papaharalampous 207
Introital Bacterial Flora—Effect of Increased Frequency of Micturition. By John M. Seddon, Andrew W. Bruce, Paul Chadwick and Donna Carter 211
Surgical Correction of Arterial Stenosis in Renal Allografts. By D. E. Osborn, J. E. Castro and R. Shackman 221
Autotransplantation of the Kidney for Fibromuscular Dysplasia of the Renal Arteries. By S. G. Ball, G. R. Giles, M. S. F. McLachlan and M. R. Lee 227
Vaginal Ureterolithotomy. By P. J. O'Boyle and N. O. K. Gibbon 231
Preliminary Communication: The Use of Bromocriptine in the Treatment of the Unstable Bladder. By D. J. Farrar and J. L. Osborne 235

ORIGINAL ARTICLES—*continued*—

PAGE

Bladder and Urethral Innervation in Multiple Sclerosis. By Jens T. Andersen and William E. Bradley 239

Chronic Bacterial Prostatitis: New Therapeutic Aspects. By A. Pfau and T. Sacks 245

The Use of Alpha-adrenergic Blockers in Benign Prostatic Obstruction. By Marco Caine, Alphonse Pfau and Shaul Perlberg 255

Random Bone Marrow Biopsy in the Staging of Carcinoma of the Prostate. By John Crisp . . 265

Amoebiasis of the Penis. By John A. Thomas and A. Joseph Antony 269

Vasoplasty: a New Technique. By V. R. Nair 275

Comparison of Sterile Bag, Clean Catch and Suprapubic Aspiration in the Diagnosis of Urinary Infection in Early Childhood. By J. D. Hardy, P. M. Furnell and W. Brumfitt 279

Comparison of Hydrophilic Polymer-coated Latex, Uncoated Latex and PVC Indwelling Balloon Catheters in the Prevention of Urinary Infection. By M. J. Tidd, J. G. Gow, J. H. Pennington, J. Shelton and M. R. Scott 285

Urological Follow-up of 99 Spinal Cord Injured Patients initially managed by Intermittent Catheterisation. By John W. Pearman 297

An Apparatus for Helmstein's Hydrostatic Pressure Treatment. By L. S. Monga 311

Composition of Bladder Stones in Rwanda. By G. Popelier, E. van den Eeckhout and W. Dekeyser 317

Trigonal Cyst in Childhood. By M. Tacciuoli, C. Laurenti and T. Racheli 323

The Effects of Drugs and Anaesthetic Agents on the Urinary Bladder and Sphincters. By P. T. Doyle and C. E. Briscoe 329

The Urethral Pressure Profile recorded by means of CO$_2$-perfusion at High Flow Rates. By R. Tscholl, F. Tettamanti and O. Wörsdörfer 337

The Urethral Closure Pressure Profile: A new technique using gas and simultaneous EMG-recording from the urethra. By Jens T. Andersen and William E. Bradley 341

Relative Contributions of Smooth and Striated Muscles to the Canine Urethral Pressure Profile. By S. A. Awad and J. W. Downie 347

Serum Antibody in Patients with Prostatic Cancer. By Richard J. Ablin 355

The Response of Lymph Node Metastases of Testicular Teratoma to Radiation Therapy. By C. J. Tyrrell and M. J. Peckham 363

Chlorhexidine for Irrigation of Vas: a Clinical Trial and the Study of Viability of Non-Motile Sperms in Post-Vasectomy Patients with Trypan Blue Uptake. By H. Y. Henry Yu, A. Halim and P. R. Evans 371

Leukoplakia associated with Renal Tuberculosis in the Chemotherapeutic Era. By Richard B. Byrd, Nicholas A. Viner, Gary H. Omell and Gary Trunk 377

Urodynamic Studies in the District General Hospital. By J. C. Crisp, N. A. Green and M. H. Ashken 383

The Ask-Upmark Kidney: A Form of Ascending Pyelonephritis? By J. H. Johnston and L. W. Mix 393

The Surgical Significance of the Proteus Stone. By W. K. Moores 399

The Thermogravimetric Analysis of Renal Stones (in clinical practice). By G. Alan Rose and C. Woodfine 403

Allograft Nephrectomy. By S. N. Sinha and J. E. Castro 413

Embolism in a Single Functioning Kidney: Report of Two Cases. By C. Selli, D. Turini and G. Berni 419

Upper Urinary Tract Obstruction: Pressure/Flow Studies in Children. By H. N. Whitfield, N. W. Harrison, T. Sherwood and D. Innes Williams 427

Preliminary Communication: Diagnosis of Gross Vesico-ureteric Reflux using Ultrasonography. By R. N. Tremewan, R. R. Bailey, P. J. Little, T. M. J. Maling, T. M. Peters and J. J. Tait . . 431

Urinary Symptoms and Total Hysterectomy. By Anne M. Jequier 437

The Real Bladder Electromyogram. By M. D. Craggs and J. D Stephenson 443

Nephrogenic Adenoma: a form of Adenomatous Metaplasia of the Bladder. A Clinical and Electron Microscopical Study. By E. A. Molland, P. A. Trott, A. M. I. Paris and J. P. Blandy . . 453

Further Studies on Effects of Irrigation Solutions on Rat Bladders. By W. E. S. Harper and L. R. Matz 463

A Reappraisal of the Pfannenstiel Incision. By David A. Griffiths 469

Live Television Transmission of Transurethral and Open Pelvic Surgery with Reproduction on a Big Screen. By E. Zingg, R. Tscholl and K. Stief 475

The Value of Prophylactic Antibiotics in Transurethral Prostatic Resection: a Controlled Trial, with Observations on the Origin of Postoperative Infection. By Michael J. Morris, David Golovsky, Michael D. G. Guinness and P. O. Maher 479

Testosterone Metabolism in Benign Prostatic Hypertrophy: *in vivo* Studies of Gestonorone Caproate and Cyproterone Acetate. By F. Orestano and J. E. Altwein 485

Detrusor and Urethral Dysfunction in Prostatic Hypertrophy. By Jens T. Andersen and William E. Bradley 493

Artificial Insemination (A.I.H.) for Sperm Antibodies and Oligozoospermia. By M. McD. Usherwood, A. Halim and P. R. Evans 499

ORIGINAL ARTICLES—*continued*—

PAGE
The Management of the Patient with Calcium Stones. By E. R. Yendt and M. Cohanim 507
Crystalluria in Normal Subjects and in Stone Formers with and without Thiazide and Cellulose Phosphate Treatment. By P. C. Hallson and G. Alan Rose 515
Size of Renal Calculi, Recurrence Rate and Follow-up. By John P. Blandy and Villis R. Marshall 525
Recurrence of Infected Calculi Following Postoperative Renal Irrigation with Stone Solvent. By Gavin Royle and Joe C. Smith 531
Primary Hyperparathyroidism—A Review of Cases in the Sheffield Area. By J. C. Hammonds, J. L. Williams and L. Harvey 539
Primary Pelvic Hydronephrosis in Children: A Retrospective Survey. By Patrick Smith, Michael Roberts, Robert H. Whitaker and Abdel Raouf Garousche 549
Reflux Induced Pelvi-ureteric Obstruction. By Robert H. Whitaker 555
Occupational Bladder Tumour Cases Identified During Ten Years' Interviewing of Patients. By Joan M. Davies, Sheena M. Somerville and D. M. Wallace 561
Inverted Papillomas of the Lower Urinary Tract. By Katherine M. Cameron and Charles H. Lupton 567
The Value of Lymphography in the Management of Bladder Cancer. By A. G. Turner, W. F. Hendry, J. S. Macdonald and D. M. Wallace 579
The Management of Deeply Infiltrating (T_3) Bladder Carcinoma: Controlled Trial of Radical Radiotherapy versus Preoperative Radiotherapy and Radical Cystectomy (First Report). By D. M. Wallace and H. J. G. Bloom 587
Radiotherapy in the Treatment of Recurrent Bladder Cancer. By W. D. Rider and D. H. Evans . . 595
Hyperthermia in the Treatment of Bladder Tumours. By R. R. Hall, V. Wadehra, J. M. Towler, J. R. Hindmarsh and P. O. Byrne 603
Treatment of Advanced Bladder Cancer with Adriamycin and 5-Fluorouracil. By R. J. Cross, R. W. Glashan, C. S. Humphrey, M. R. G. Robinson, P. H. Smith and R. E. Williams 609
The Endemic Bladder Stones of Indonesia—Epidemiology and Clinical Features. By Kamardi Thalut, Ahmad Rizal, J. G. Brockis, R. C. Bowyer, T. A. Taylor and Z. S. Wisniewski 617
Distension Therapy for the Unstable Bladder: Later Results including an Assessment of Repeat Distensions. By P. D. Ramsden, J. C. Smith, M. Dunn and G. M. Ardran 623
Clinical and Experimental Studies on the Action of Prostaglandins and their Synthesis Inhibitors on Detrusor Muscle *in vitro* and *in vivo*. By M. I. Bultitude, N. H. Hills and K. E. D. Shuttleworth 631
Anti-reflux Surgery in the Congenital Neuropathic Bladder. By J. H. Johnston, S. R. Shapiro and G. G. Thomas 639
The Assessment of Sphincteric Activity in Patients following Trans-sphincteric Urethral Reconstruction. By Robert D. Schwarz, John W. Foote, Douglas D. Morehouse and Kenneth J. Mackinnon 643
Division of the External Urethral Sphincter in the Neuropathic Bladder: A Twenty Years' Review. By J. Cosbie Ross, N. O. K. Gibbon and G. Sham Sunder 649
An Assessment of Surgical Treatment of Vesical Outlet Obstruction in Spinal Cord Injury: A Review of 471 Cases. By J. Dermot O'Flynn 657
Urodynamics in the Prune Belly Syndrome. By H. M. Snyder, N. W. Harrison, H. N. Whitfield and D. Innes Williams 663
Anterior Detrusor Tube Repair for Urinary Incontinence in Children. By D. Innes Williams and Howard Snyder 671
A Simple Artificial Implantable Sphincter. By Michael Rosen 675
Excretion Urography in the Investigation of Prostatism. By P. H. Abrams, J. Roylance and R. C. L. Feneley 681
Hypothermic Prostatic Resection. By A. Serrao, M. K. Mallik, P. A. Jones, W. F. Hendry and J. E. A. Wickham 685
Lymphography and Pelvic Lymphadenectomy in Carcinoma of the Prostate. By E. P. N. O'Donoghue, P. Shridhar, T. Sherwood, J. P. Williams and G. D. Chisholm 689
Urethroplasty in Context. By J. P. Blandy, S. Wadhwa, M. Singh and G. C. Tresidder . . . 697
Hypospadias—Problems of Postoperative Fistulae Formation and a Modified 2-Stage Procedure to Reduce These. By P. J. B. Smith, P. L. G. Townsend, R. W. Hiles and J. R. Bryson . . . 703
Plasma Gonadotrophic Hormones, Testicular Biopsy and Seminal Analysis in the Men of Infertile Marriages. By J. P. Pryor, R. C. B. Pugh, K. M. Cameron, J. R. Newton and W. P. Collins. 709

SHORT CASE REPORTS—

Duodenal and Common Bile Duct Obstruction with a Pyelo-duodenal Fistula caused by Renal Calculous Pyonephrosis. By K. P. Boardman 6
Complete Avulsion of the Renal Pedicle due to Blunt Injury to Abdomen. By D. G. Jenkins and K. G. Gupta 12

SHORT CASE REPORTS—*continued*—

PAGE
Midline Ensheathed Ureters. By R. J. Salem and R. J. Luck . . . 18
Ureteric Invasion by Endometriosis. By Stanley Way and J. R. Young . . . 38
Recurrent Spontaneous Rupture of the Urinary Bladder. By F. R. Jackaman . . . 54
Recurrent Transitional Cell Carcinoma complicating Ileal Conduit. By D. M. Allan . . . 60
Female Hypospadias. By J. Fischelovitch and M. Ben-Bassat . . . 72
Posterior Urethral Valves in Siblings. By Amicur Farkas and Donald G. Skinner . . . 76
Accessory Vas Deferens: A Case Report. By V. R. Mysorekar . . . 82
A Complication of Nephrectomy by the Supracostal Approach. By Gordon Williams and J. E. Castro 106
Bilateral Renal Carcinomas Treated Operatively. By Stefan Wesolowski . . . 118
Lymphocele following Renal Transplantation: an Unusual Cause of Urinary Retention. By Martin Schiff, Jr. and Robert A. Feldman . . . 122
Peritoneal Tuberculosis with Ureteric Obstruction, Mimicking Retroperitoneal Fibrosis. By P. G. Bentley and D. R. Higgs . . . 170
Malignant Testicular Lymphoma in Brothers. By B. L. S. Gallagher and A. I. Hashmat . . . 210
Localised Primary Amyloidosis of the Bladder. By Richard A. Blath and James G. Bucy . . . 219
Appendix Ureteroplasty. By R. W. Weinberg . . . 234
Ectopia Vesicae Complicated by Squamous Cell Carcinoma. By S. Gupta and I. M. Gupta . . . 244
An Osteolytic Lesion as a Presentation of Bladder Carcinoma. By J. G. W. Feggetter . . . 254
Posterior Urethral Duplication. By D. Osborne and J. C. Gingell . . . 264
Regression of Penile Metastases of Prostatic Carcinoma with Cyproterone Acetate Therapy. By R. M. Jameson . . . 268
Tuberculosis of the Penis. By A. Sriman Narayana, D. G. Kelly and F. A. Duff . . . 274
Congenital Urethral Polyp in a Child. By F. H. Bagley and A. I. Davidson . . . 278
A Knot in the Urethra. By Wim Oosterlinck and Guy Renders . . . 284
Ileal Replacement of Ureter of Solitary Kidney: 22-year follow-up. By S. Wesolowski . . . 292
Hyperparathyroidism and Sodium Cellulose Phosphate. By J. R. Condon, R. A. V. Milsted and J. R. Nassim . . . 316
Ureterocalyostomy. By M. G. McLoughlin . . . 328
Primary Vaginal Stone. By S. K. Sharma, S. N. Wadhwa and J. S. Chabra . . . 336
Reversible Neuromyopathy in Hypernephroma. By D. M. Fraser, A. J. Franks and I. W. Campbell 340
Leukoplakia of the Male Urethra. By P. Vijayan, P. B. Clark and C. K. Anderson . . . 346
Unilateral Renal Hypertension following Major Trauma. By C. M. Ludgate and G. S. Watson . 362
Leukoplakia of Renal Pelvis. By J. Fischelovitch and I. Avidor . . . 376
Rupture of a Bladder Diverticulum in Multiple Sclerosis. By R. B. Smith and M. G. Kettlewell . 382
Free Supernumerary Kidney. By K. Sasidharan, A. S. Babu, M. Mohan Rao and H. S. Bhat . 388
Pelvic Lipomatosis presenting as Acute Ureteric Obstruction. By S. Kupelian and M. R. G. Robinson 389
Malignant Melanoma of the Male Urethra. By Y. Terada and H. Takayasu . . . 390
Contralateral Ureteric Metastasis from Renal Carcinoma. By M. A. Hughes, D. G. Arkell, P. Dawson-Edwards and J. R. Geddes . . . 402
Appendiceal Granuloma causing Bilateral Hydronephrosis and Macroscopic Haematuria. By K. Shimada, T. Katsumi and H. Fujita . . . 418
Filariasis Penis. By Shyam Prasad . . . 426
Appendico-vesical Fistula due to an Appendix Abscess with associated Goblet Cell Carcinoid of the Appendix. By M. Di Paola and W. S. Stockwell . . . 436
Familial Profile of Transitional Cell Carcinoma. By S. K. Sharma, B. C. Bapna and S. M. Singh . 442
Long Survival after Vaginal Sarcoma Botryoides. By A. E. Stuart and J. Magri . . . 452
A Gynaecological Presentation of Phaeochromocytoma of the Urinary Bladder. By A. S. Whyte and A. Dick . . . 468
Urinary Retention due to Congenital Posterior Urethral Polyp in a Boy. By A. Ipiéns Aznar and J. M. Martinez-Peñuela V . . . 478
Obstructing Prostatic Urethral Calculi. By R. K. Vinson and S. A. Koff . . . 492
Testicular Metastasis from Prostatic Carcinoma. By N. P. Silverton . . . 498

BOOK REVIEWS . . . 89, 157, 293, 391, 504

BOOKS RECEIVED . . . 90, 158, 392

ANNOUNCEMENTS . . . 90, 158, 294, 504

ABSTRACTS FROM CURRENT UROLOGICAL LITERATURE . . . 296, 505

PAGE

ABSTRACTS OF THE PROCEEDINGS OF THE UROLOGICAL SOCIETY OF AUSTRALASIA, 28TH ANNUAL GENERAL MEETING, SYDNEY, 1975 145

ERRATA 91

CURRENT UROLOGICAL LITERATURE: SELECT BIBLIOGRAPHY . . . . . i, xli

AUTHOR INDEX 719

SUBJECT INDEX 724

LIBRARY

Contents

ORIGINAL ARTICLES

1 **Uric Acid Disorders in Patients with Calcium Stones**
A. Hodgkinson

7 **Urinary Citrate Excretion in Stone-formers and Normal Controls**
S. G. Welshman and M. G. McGeown

13 **The Elastic Component of Normal and Dilated Ureters in Children: Chemical and Histochemical Characterisation**
F. Pagano, G. Passerini, R. Cortivo, D. Daga-Gordini and G. Abatangelo

19 **Experience with the Ileal Ureter**
Hessein A. Amin

27 **Endometriosis Mimicking Ureterolithiasis**
Y. M. Traub, J. Fischelovitch, A. Neri and E. Lubin

31 **Re-implantation of the Ureter**
Philip Clark and R. U. Hosmane

39 **First Report on the Standardisation of Terminology of Lower Urinary Tract Function**
Produced by the International Continence Society, February, 1975

43 **Innervation of the Muscle of the Bladder in the Rat**
A. D. Hoyes, R. Bourne and B. G. H. Martin

55 **Single Dose Intravesical Thiotepa as an Adjuvant to Cystodiathermy in the Treatment of Transitional Cell Bladder Carcinoma**
K. G. Burnand, P. J. R. Boyd, M. E. Mayo, K. E. D. Shuttleworth and R. W. Lloyd-Davies

61 **Studies on the Chemical Nature of Urinary Chemiluminescence**
G. Alan Rose

73 **The Effect of Bromocriptine in Patients with Benign Prostatic Hypertrophy**
D. J. Farrar and J. S. Pryor

77 **A Study of Concentrations of Trimethoprim-Sulphamethoxazole in the Human Prostate Gland**
N. F. Dabhoiwala, A. Bye and M. Claridge

83 **Badenoch's Pull-through Operation for Urethral Stricture**
G. H. Tilak, H. C. Dhayagude and S. S. Joshi

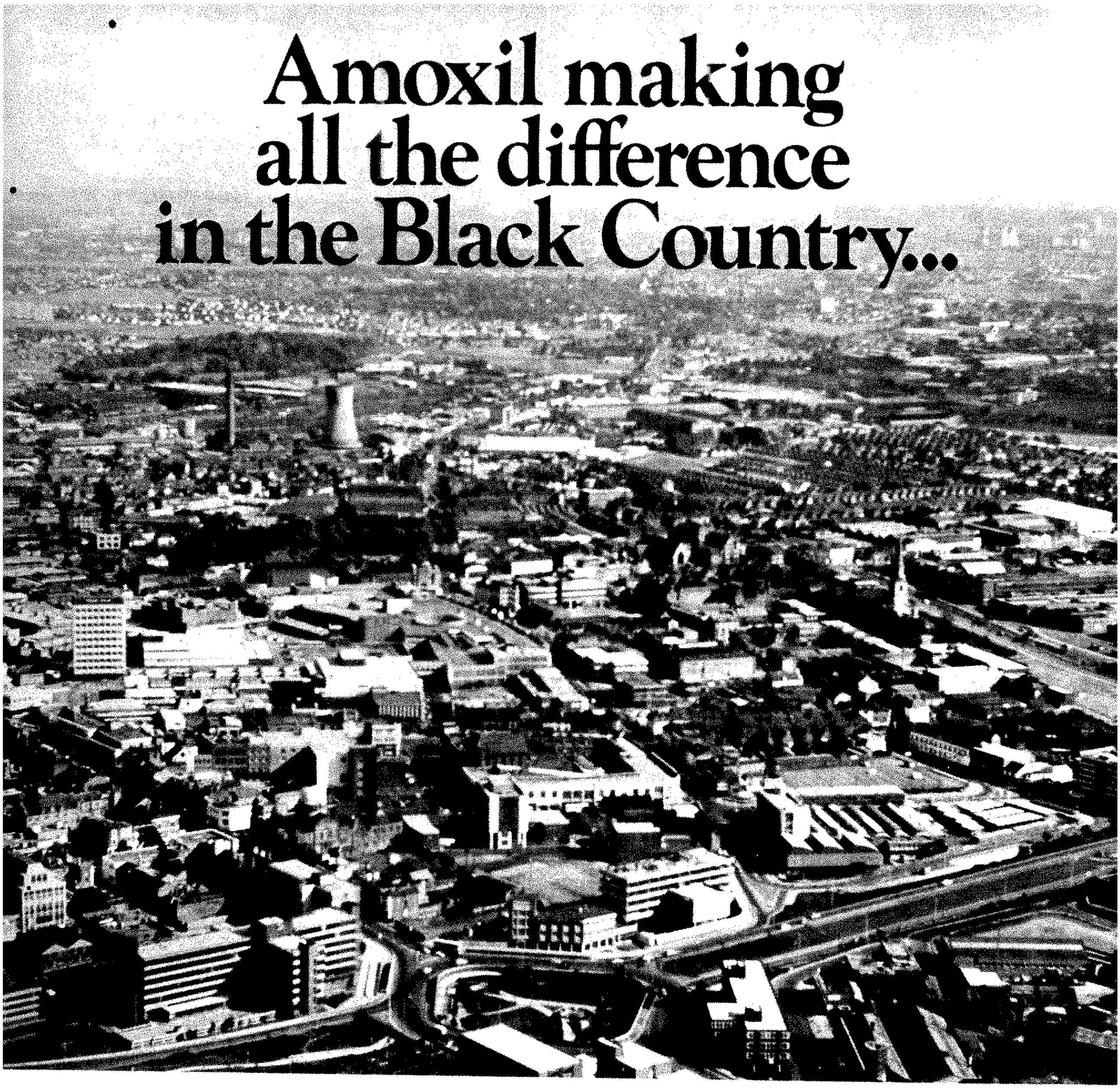
SHORT CASE REPORTS

6 **Duodenal and Common Bile Duct Obstruction with a Pyelo-duodenal Fistula caused by Renal Calculous Pyonephrosis**
K. P. Boardman

12 **Complete Avulsion of the Renal Pedicle due to Blunt Injury to Abdomen**
D. G. Jenkins and K. G. Gupta

ISSN 0007-1331

Amoxil making all the difference in the Black Country...

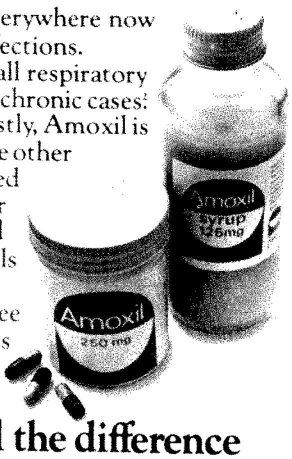


And throughout Britain. Because doctors everywhere now recognise the advantages of Amoxil in respiratory infections.

Amoxil ensures faster relief of symptoms[1] for all respiratory patients and longer periods free from infection for the chronic cases[2].

Three main factors are responsible for this. Firstly, Amoxil is more completely absorbed into serum[3]. Secondly, unlike other antibiotics it penetrates equally well through inflamed and uninflamed bronchial membrane barriers[4] to clear even the most entrenched pockets of infection[5]. And thirdly, extensive studies have shown that Amoxil kills bacteria more rapidly than other antibiotics[6,7].

These three factors, together with a trouble-free dosage, contribute to the Amoxil difference which is appreciated by doctors and patients everywhere.



makes all the difference in respiratory infections everywhere.

itioner (1974), 212, 123.
notherapy (1973), 18, (Suppl.) (19), 1.
led. J., (1972), 3, 13.
rpta Med. I.C.S. (1974) No. 326, 130.
Med. J., (1973), 47, 7[illegible].
nicrob. Ag. Chem. (1975), 7, (2), 179.
biotics under the Microscope. A film
r available to the medical profession.

escribing information on Amoxil (regd.),
illin, is available from: Bencard,
Vest Road, Brentford, Middlesex.

Bencard

18 **Midline Ensheathed Ureters**
R. J. Salem and R. J. Luck

38 **Ureteric Invasion by Endometriosis**
Stanley Way and J. R. Young

54 **Recurrent Spontaneous Rupture of the Urinary Bladder**
F. R. Jackaman

60 **Recurrent Transitional Cell Carcinoma complicating Ileal Conduit**
D. M. Allan

72 **Female Hypospadias**
J. Fischelovitch and M. Ben-Bassat

76 **Posterior Urethral Valves in Siblings**
Amicur Farkas and Donald G. Skinner

82 **Accessory Vas Deferens: A Case Report**
V. R. Mysorekar

89 BOOK REVIEWS

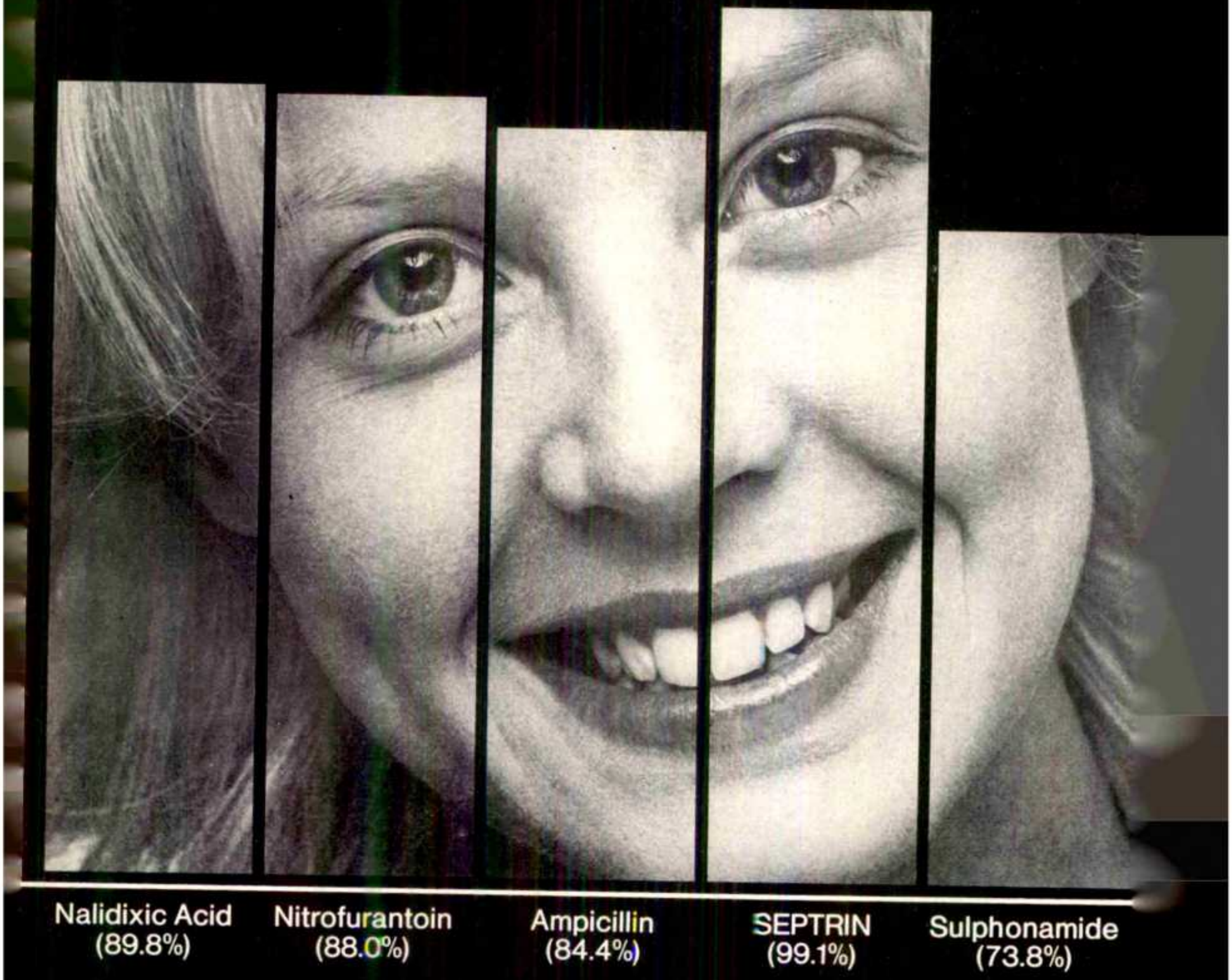
90 BOOK RECEIVED

90 ANNOUNCEMENT

91 ERRATA

i CURRENT UROLOGICAL LITERATURE: SELECT BIBLIOGRAPHY

A 99.1% chance of success in U.T.I.



The chart above shows the percentage sensitivities of isolates from acute urinary infections against five commonly-used antibacterials. (From an *in-vitro* study involving 173 general practitioners). SEPTRIN was superior to all other oral antibacterials tested, with 99.1% of urinary pathogens sensitive.

J int med Res (1974), **2**, 40

come
contains
prim and
ethoxazole.
ESCRIBING
TION IS AVAILABLE
JEST.
e Medical Division
lcome Foundation Ltd
nsted, Herts

SEPTRIN first
TRADE MARK
# in urinary tract infection

Instructions to Authors

The *British Journal of Urology* welcomes original contributions on urological subjects from all parts of the world. The papers are accepted for consideration on the understanding that their contents have not been published in whole or in part elsewhere and that they are subject to editorial revision.

Any paper may be sent initially to a member of the Editorial Committee for comment and advice on its being suitable to be considered for publication.

A leaflet showing the criteria used in the assessment of papers submitted for consideration is available from the Editor on request.

Authors should supply their qualifications, main appointment, and the name and address of the hospital or the laboratory.

Please indicate name and address to which requests for reprints should be made.

Format and content of papers

The text of articles submitted for publication should be typewritten in double-spacing on paper sheet size 22 × 32 cm (A4). There should be a minimum margin of 3 cm all round. The pages should be numbered.

Reports on clinical or laboratory investigation should as far as possible be organised into the following main sections: (1) Introduction, (2) Objective(s), (3) Patients or Materials, (4) Procedures or Methods, (5) Findings or Results, (6) Discussion and (7) Conclusions with (8) a Summary at the end.

Nephrology. Papers on disorders of renal function of interest to the urological surgeon are welcome.

Ethics. When relevant, authors must include a statement on the ethical aspects of their research.

Reports of clinical cases should consist of the following sections: (1) Introduction, (2) Case Reports and (3) Comment with (4) a Summary at the end.

Reports on single cases. Papers reporting a single case are considered for publication as full papers only when the case has definite instructional value. The Introduction and Discussion should not be disproportionate to the case presentation. *An abbreviated version suitable for publication as a Short Case Report as an alternative must also be submitted.*

In all full papers the literature should be summarised as concisely as is consistent with establishing the necessary basis for new material. Discussions and Conclusions should be strictly limited to the results presented. Recapitulation from previous sections should be avoided whenever possible. Summaries should be composed of very brief statements about each of the main sections.

Headings. The relative importance of sub-headings should be clearly indicated.

Numbers. All numbers should be shown as figures rather than as words.

References. *The accuracy of references is the responsibility of the author.* Only papers closely related to the author's work should be referred to; exhaustive lists should be avoided. *References in the text* should be quoted by the author's name(s) and year of publication. Unless there are more than 3 authors, all the names should be stated at the first reference; if there are more than 3 authors only the first author plus *et al.* is used. In subsequent references to the same paper, *et al.* is used if there are more than 2 authors. *The list of references at the end of the paper* should be in alphabetical order. *References to journals* should include the name(s) and initials of the author(s), year, title of paper, name of journal in full, volume number and the numbers of the first and last pages, *References to books* should include the name and initials of the author, year, title of book, number of edition. city of publication, name of publishing house, and page number(s).

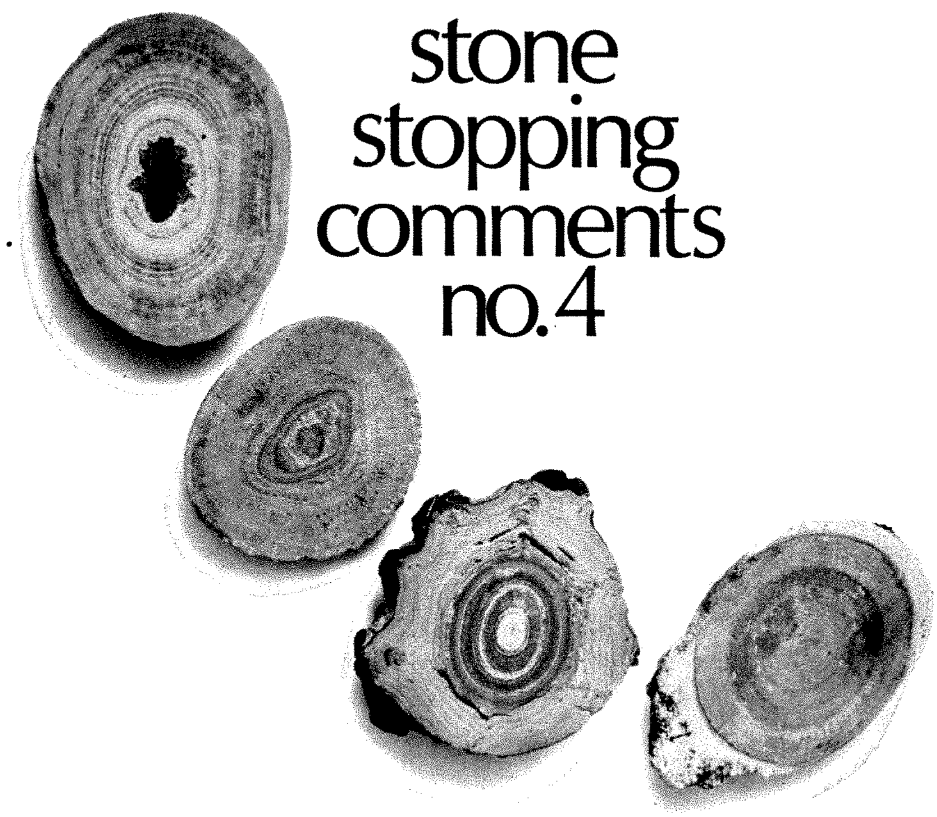
Illustrations. Photographs and radiographs should be submitted in the form of *matt* prints of a size no larger than 17·5 × 12·5 cm and no smaller than 9 × 6·5 cm. All figures should be sent unmounted. The number of the figure, the name of the author and the "top" of the illustration should be indicated lightly in pencil on the back. The magnification of micro-photographs should be stated. Graphs and diagrams should be drawn in Indian ink. *Lettering and figures must be indicated only on a transparent cover.* Legends to figures should be typewritten on a separate sheet of the manuscript. Tables, unless they are very small, should also be typewritten on separate sheets. The position of illustrations and tables should be indicated in the margin of the text.

There is no charge to contributors for the printing of black-and-white illustrations on papers accepted for publication. Illustrations in colour may be accepted at the discretion of the Editor provided he is of the opinion that these are necessary for the improvement of the article. The author may be required to pay for the extra cost involved by the reproduction in colour.

Reprints

25 offprints are supplied to the first named author only, free. Forms for ordering offprints will be sent with the proofs for correction; the order form should be returned with the corrected proofs within 7 days.

Continued on page vii



stone stopping comments no.4

In a recent study[1] measurements of ^{47}calcium and of urinary calcium excretion were made in 125 cases of urolithiasis (78 solitary stone, 47 recurrent).

The authors found that 57 out of 60 patients with hypercalciuria showed raised absorption of ^{47}Ca, whereas 49 out of 106 patients showing similar hyperabsorption of calcium had *normal* calcium excretion. The authors concluded that "...a majority of stone formers, whether they are hypercalciuric or not, absorb calcium excessively from the intestine and this is more prevalent in cases of recurrent urolithiasis."

As a sequel to investigation 1, the same authors[2] studied the effect of Sodium Cellulose Phosphate on intestinal calcium uptake. In comparison to a low calcium, low oxalate diet; "Sodium Cellulose Phosphate can significantly diminish the absorption of calcium from the intestine; there is concomitant diminution of urinary calcium excretion. The plasma levels of the divalent cations do not appear to be influenced by this therapy."

Dosage in this study was varied to evaluate therapeutic effect. "Five grams reduced the intestinal calcium by as much as 85% and even a 1 g dose resulted in a 50% reduction... Such a dose (5 g), however, is probably essential when it is considered that the substance will ordinarily be dispersed throughout a semi-solid food bolus." Optimum administration time was considered to be 5 g t.i.d. at meal times, or within 1 hour after food.

In terms of side-effects and toxicity, the authors stated "Serum levels of calcium and phosphorus were not altered in any of the patients even when the substance had been taken for a period as long as 7 years in a dose of 5 g 3 times daily." There was no diarrhoea or intestinal disturbance, and patients found SCP reasonably palatable and easy to take.

Presentation
Whitish cream powder packaged in paper aluminium polythene single-dose sachets of 5 g each.
Supplied in packs of 100.

References
1. Brit J Urol, (1974) **46**: 377-384.
2. Brit J Urol, (1974) **46**: 385-392.

Whatman
Sodium Cellulose Phosphate
to reduce dietary calcium absorption.
Full prescribing information is available on request.

Whatman®
Whatman Biochemicals Limited,
Springfield Mill, Maidstone, Kent.
Telephone: Maidstone 61688/9 Telex: 96113

Travelling Fellowship

The British Association of Urological Surgeons offers a Travelling Fellowship of £250 based on the best paper published in the *British Journal of Urology* in the preceding year including those papers presented at the British Association of Urological Surgeons Annual Meeting.

Candidates for the prize must be Fellows of one of the Royal Colleges of Surgeons in the British Isles, Canada, Australasia or South Africa who are in the course of urological training or who have obtained consultant posts within 10 years of the date of submission of the paper.

The Fellowship will be awarded for the best paper published in the Journal from the April issue of one year to the February issue of the following year.

Authors of papers with multiple authorship should indicate which one of their number should be awarded the Fellowship in the event of their contribution being selected.

Three assessors will be appointed by the Council to make recommendations on the award of the Fellowship. The Council reserves the right not to make an award in any one year.

The award will be announced at the June meeting of the Association.

Short Case Reports

Brief reports (preferably with 1 and not more than 2 illustrations) of unusual cases not published elsewhere may be submitted as summaries of not more than 200 words for consideration for publication as Short Case Reports. They should comprise (1) a Title, (2) Case description and (3) a brief Comment. The authors and references are each limited to 3. The titles of these reports will usually be recorded in Index Medicus and by MEDLARS.

Preliminary Communications

Preliminary communications of original work may be submitted as short papers. The communication should be divided into 4 sections: (1) Objectives, (2) Materials and Methods, (3) Preliminary results, (4) Interpretation or Significance of Results.

Discussion of Papers

Questions or criticisms concerning recently published paper may be sent to the Editor, who will refer them to the authors. The readers' comments and authors' replies may subsequently be published together.

There is no other correspondence section in the Journal.

Suggested Projects for Urological Research

Clinicians who have ideas for research projects, but have no opportunity for carrying them out, may submit them for publication in the above section. The communication should not be longer than 500 words. References will be limited to 6.

Abstracts from Current Urological Literature

Urologists who are willing to undertake abstracting of urological articles appearing in other journals should communicate with the Assistant Editor, Mr. W. Selby Tulloch, at the Department of Urology, Western General Hospital, Edinburgh, EH4 2XU.

Addresses

With the exceptions noted below, all editorial communications, including books for review, should be addressed to the Editor, Mr. W. Keith Yeates, at the Department of Urology, Newcastle General Hospital, Newcastle upon Tyne, NE4 6BE.

Preliminary Communications on Research Projects and *Suggested Projects for Urological Research* should be submitted to the Assistant Editor, Mr G. D. Chisholm, at The Urology Unit, Hammersmith Hospital, Royal Postgraduate Medical School, London, W12 0HS.

Short Case Reports (presented as described above) should be sent to the Assistant Editor, Mr W. F. Hendry, Institute of Urology, University of London, 172 Shaftesbury Avenue, London, WC2H 8JE.

Communications concerning the Abstract Section should be sent to the Assistant Editor, Mr W. Selby Tulloch, at the Department of Urology, Western General Hospital, Edinburgh, EH4 2XU.

Publishing, Advertisement and other enquiries: E. & S. Livingstone, Longman Group Ltd., Journals Division, Longman House, Burnt Mill, Harlow, Essex CM20 2JE.

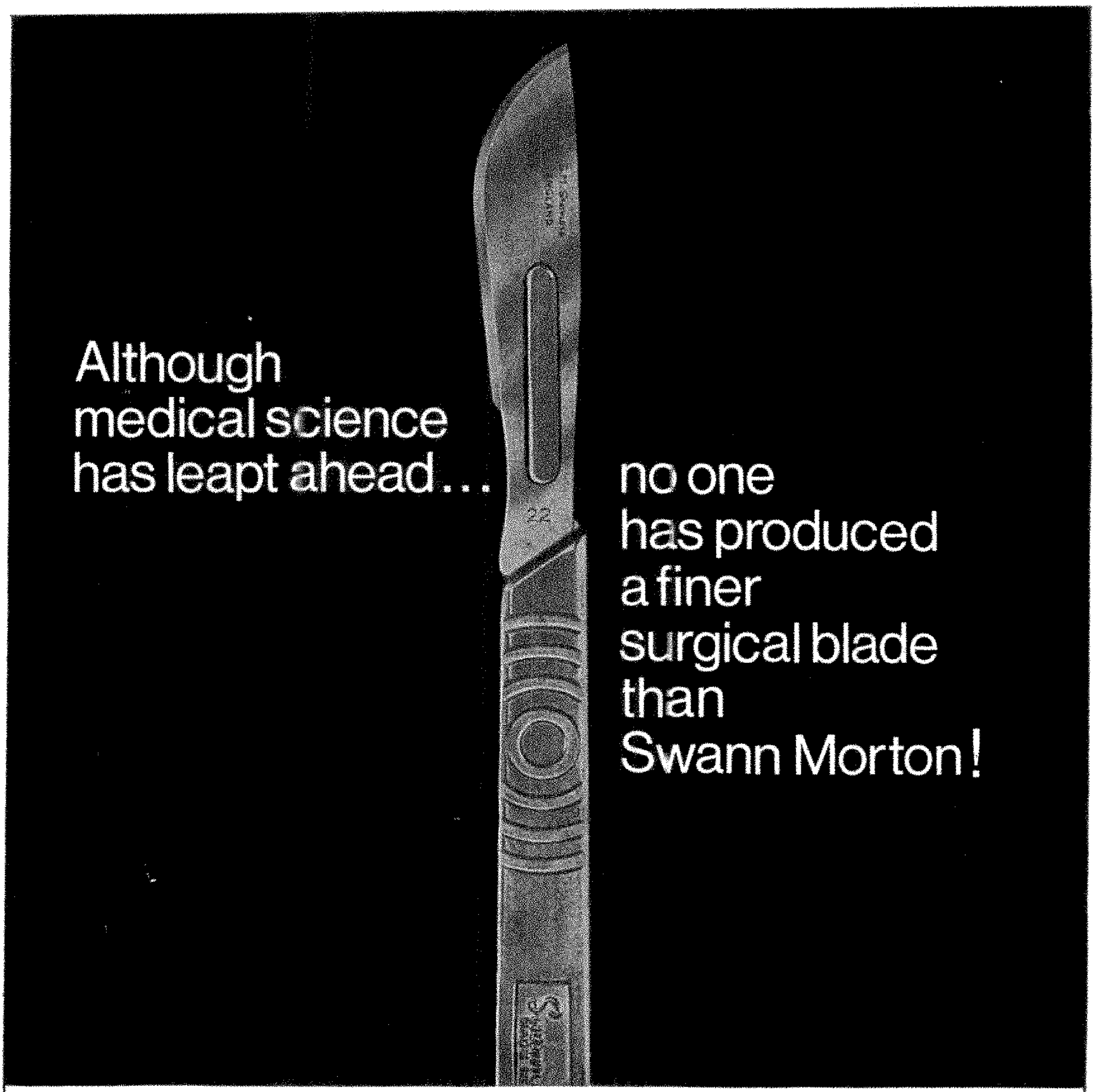
Subscriptions

The Journal is published in February, April, June, August, October and December. Subscription £17·00 (U.S.A. $45.00) per annum, post free. Single copies £3·00 (U.S.A. $9.00) each. Previous volumes and parts of volumes (if available) may be obtained from the publishers, price £6.00 per volume or 75p for single parts.

Subscription enquiries: Messrs E. & S. Livingstone, Journals Division, 43/45 Annandale Street, Edinburgh, EH7 4AT.

Subscriptions for U.S.A. should be sent to The Williams and Wilkins Company, 428 East Preston Street, Baltimore, Maryland, U.S.A.

All rights reserved. No part of this publication may be reproduced, stored in a retrieval system, or transmitted in any form or by any means, electronic, mechanical, photo-copying, recording or otherwise, without the prior permission of the copyright owner.



Swann-Morton, the world's largest producers of surgical blades have kept abreast of the extremely high demands in surgical fields. Safe, stable and economical, their blades are sterilized by gamma radiation packed in quick peel foil envelopes and of a superb quality yet to be beaten.

STERILIZED
CARBON STEEL BLADES

STERILIZED
STAINLESS STEEL BLADES

STANDARD
CARBON STEEL BLADES

STERILE DISPOSABLE
STITCH CUTTERS

SURGICAL HANDLES

AUTOCLAVABLE PLASTIC
SURGICAL HANDLES

Swann-Morton

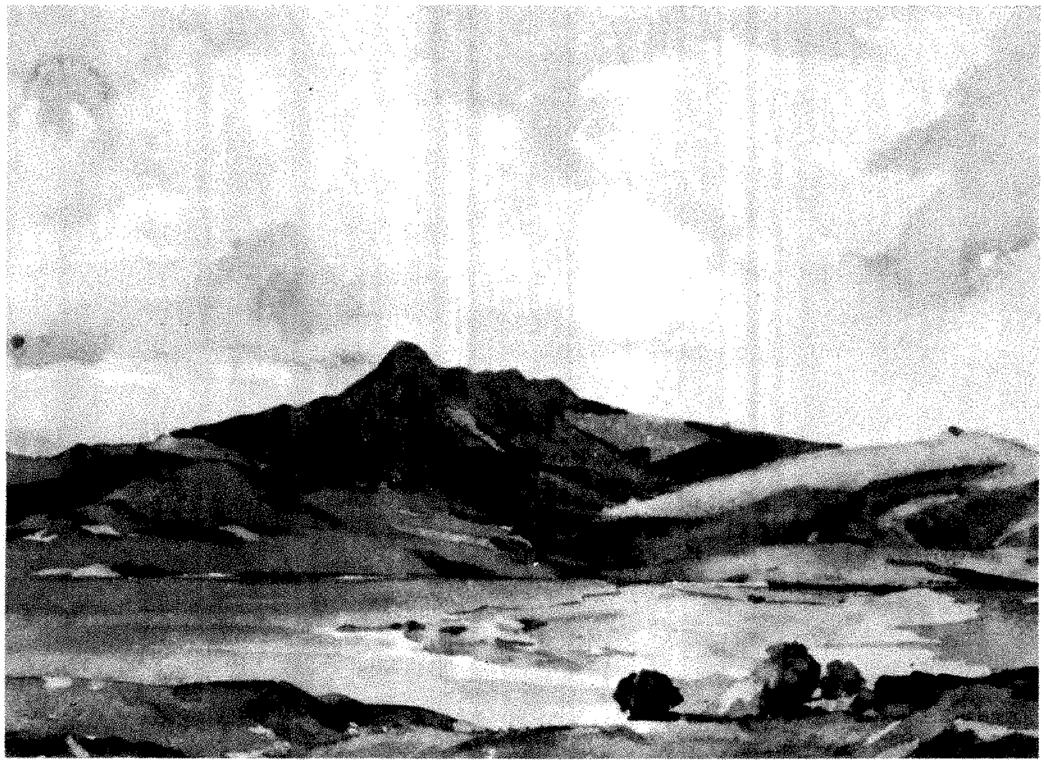
Surgical Blades

SWANN-MORTON LIMITED
PENN WORKS, OWLERTON GREEN,
SHEFFIELD S6 2BJ. ENGLAND

in radiography

conray contrast media

provide a distinctly better prospect all round



There is a wide range of 'Conray' formulations and almost certainly one to meet your special requirements however exacting they may be. 'Conray' provides wide margins of safety for the patient and superb visualization in a comprehensive range of radiographic procedures.

'Conray' Contrast media are preparations of meglumine iothalamate, sodium iothalamate or combinations of the two.

Further information on 'Conray' 280, 'Conray' 325, 'Conray' 420, Cardio-'Conray', Retro-'Conray' and Gastro-'Conray' supplied on request.
'Conray' is a trade mark of Mallinckrodt Inc.

May & Baker Ltd.
Dagenham, Essex RM10 7XS

M&B May & Baker

A member of the Rhône-Poulenc Group of Companies

MA 4334

Handbuch der Urologie
Encyclopedia of Urology
Editors: L. Andersson,
R. F. Gittes, W. E. Goodwin,
W. Lutzeyer, E. Zingg

Band 13, Teil 3: Operative Urology III

R. KÜSS, C. CHATELAIN

Surgery of the Ureter

Translated from the French by A. Walsh

233 figures with more than 400 illustrations
X, 337 pages. 1975 Cloth DM 240,—; US $98.40
Subscription price Cloth DM 192,—; US $78.80
ISBN 3-540-07128-8

Contents: Introduction. — General Considerations. — The Surgical Approach to the Ureter. — Ureterolysis. — Ureterotomy. — Ureteral Anastomosis. — Ureterectomy. — Replacement Ureteroplasty. — Urinary Diversion Utilising the Ureter. — Surgery of Vesico-Uretero-Renal Reflux. — Surgery of Megaureter. — Surgery of Ureterocele. — Surgery of Retrocaval Ureter. — Surgery of the Ureter in Kidney Transplantation. — General Conclusions.

Band 13, Teil 1

Operative Urology I

By W. Bischof, P. Bischoff, C. Franksson, R. Frey, J. H. Harrison, J. Hellström, W. Tönnis
183 figures. XII, 460 pages (287 pages in German). 1961
Cloth DM 230,—; US $94.30
Subscription price Cloth DM 184,—; US $75.50
ISBN 3-540-02692-4

Band 13, Teil 2

Operative Urology II

By Th. Burghele, R. F. Gittes, V. Ichim, J. J. Kaufman, A. N. Lupu, D. C. Martin
132 figures. XI, 256 pages. 1970.
Cloth DM 165,—; US $67.70
Subscription price Cloth DM 132,—; US $54.20
ISBN 3-540-05142-2

Springer-Verlag
Berlin
Heidelberg
New York

Prices are subject to change without notice

our enlarged range

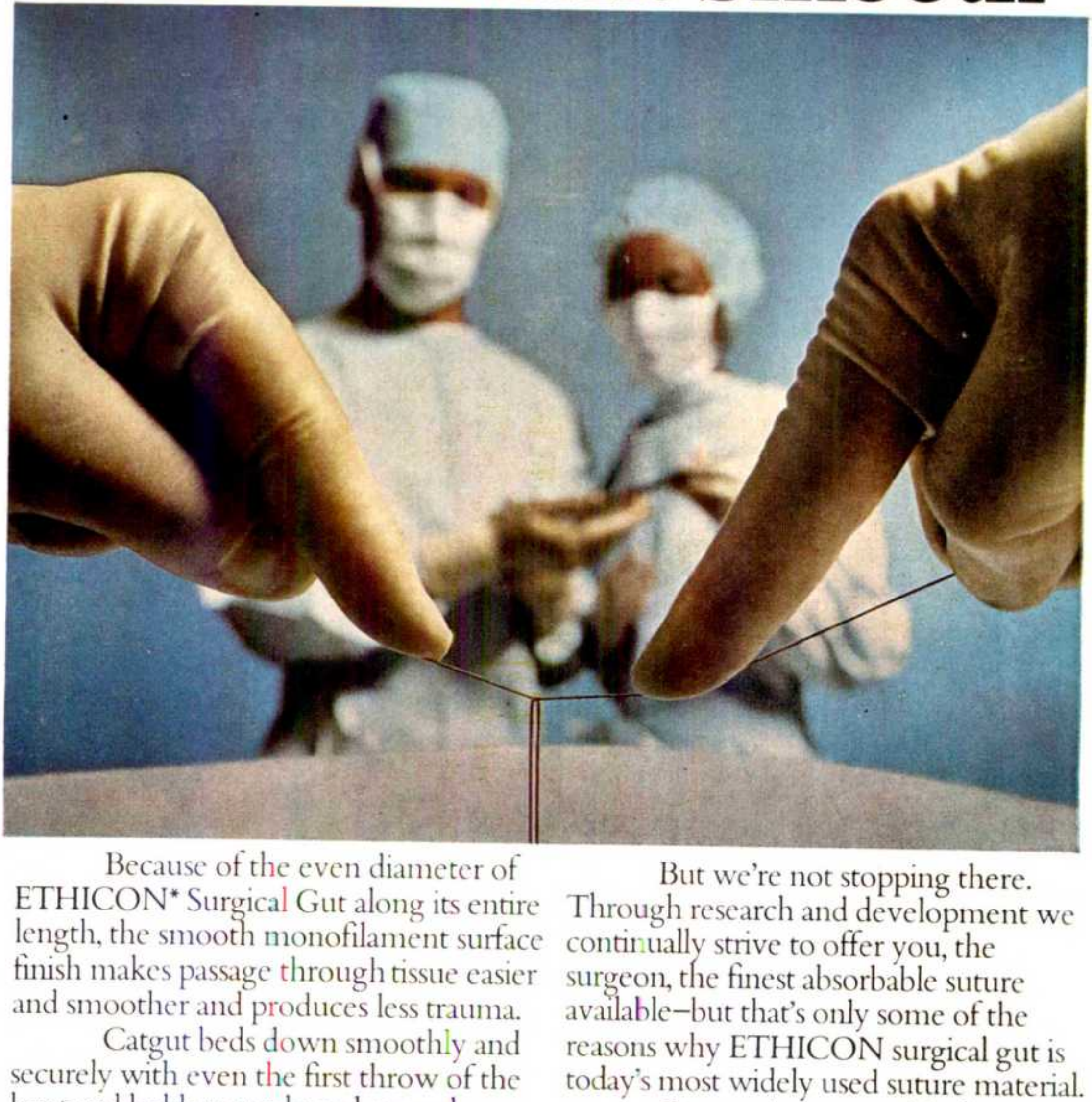
. . . now offers you a triple choice* of price conscious, quality surgical instruments that is hard to match anywhere

The Medical Supply Association Ltd
Bourne Road Bexley Kent
Telephone Crayford 529114
Branches throughout the UK

*Simal, Heljestrand and MSA brands

msa instruments in a big way

Monofilament Smooth



Because of the even diameter of ETHICON* Surgical Gut along its entire length, the smooth monofilament surface finish makes passage through tissue easier and smoother and produces less trauma.

Catgut beds down smoothly and securely with even the first throw of the knot and holds securely and strongly with standard surgical knots.

But we're not stopping there. Through research and development we continually strive to offer you, the surgeon, the finest absorbable suture available—but that's only some of the reasons why ETHICON surgical gut is today's most widely used suture material.

Catgut places a world of experience at your fingertips.

ETHICON
Trademark

When the difference is between being sure and being absolutely certain.

PLR 0508/5002

© ETHICON Ltd 1976 *Trademark

British Journal of Urology (1976), **48**, 1-5 ©

Uric Acid Disorders in Patients with Calcium Stones

A. HODGKINSON
Medical Research Council, Mineral Metabolism Unit, The General Infirmary, Leeds

An association between uric acid metabolism and calcium oxalate stones has been suspected for some years but the precise nature of the relationship is not yet clear. Uric acid is known to promote the crystallisation of calcium oxalate *in vitro* (Mayer *et al.*, 1968; Robertson, Peacock and Nordin, 1971) and there have been reports that some gouty patients form calcium, rather than uric acid stones (Gutman and Yü, 1968; Prien and Prien 1968). Hyperuricaemia has frequently been observed in primary hyperparathyroidism (Mintz *et al.*, 1961; Scott, Dixon and Bywaters, 1964; Ory, Hisey and Redmond, 1970) and hyperuricaemia or hyperuricosuria, or both, have been reported in patients with idiopathic calcium stones (Mayer *et al.*, 1968; Smith *et al.*, 1969; Mugler 1970; Dent and Sutor 1971; Coe and Cavalach, 1974; Hartung and Bergmann, 1974).

The present study was undertaken to determine the incidence of uric acid disorders among stone patients in the Leeds area and the extent to which these abnormalities are due to the diet or other causes.

Methods

Observations were made on 132 male patients, aged 20 to 55 years, with a history of calcium-containing urinary tract stones and on 24 healthy men with a similar age range. Patients with hypercalcaemia or cystinuria were excluded from the study. The composition of the patient's stones was known in 86 cases; in the remaining cases, the evidence for calcium-containing stones was based on the patient's history, the presence of radio-opaque shadows in the kidney or ureter and absence of cystinuria. Approximately 40% of the patients had a daily excretion of calcium on a normal diet, which exceeded 8·0 m mol (320 mg).

Blood samples were taken between 09.00 and 10.00 hours with the subject in a non-fasting or fasting state. Urine was collected in polythene containers to which had been added 1 ml of 0·35 m.mol/l (20 g/100 ml) chlorhexidine gluconate (Hibitane). 24-hour urine collections were made while the subjects were following their normal daily activity and eating a diet of their own choice. Fasting urine samples were collected, without preservative, between 08.00 and 10.00 hours from patients who had not eaten since 22.00 hours on the previous night.

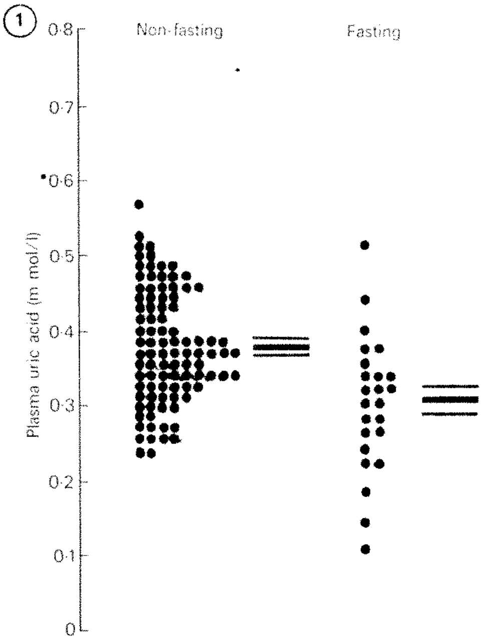
Uric acid was determined enzymatically with uricase (Sigma Chemical Co.). Calcium, phosphorus and creatinine were determined by automatic colorimetry (Technicon Auto Analyzer Methods, AAII-03; AAII-04 and AAII-11, respectively). The composition of the stones was determined by quantitative chemical analysis (Hodgkinson, 1971) and oxalic acid was estimated colorimetrically after reduction to glycolic acid with zinc (Hodgkinson and Williams, 1972).

Results

Effect of fasting on Plasma Uric Acid Levels

Figure 1 shows the plasma uric acid levels in 95 normal men, 1 to 2 hours after taking breakfast and in 24 men who had fasted for approximately 12 hours. The mean non-fasting value was 0·380 mmol/l (6·4 mg/100 ml) compared with 0·306 mmol/l (5·2 mg/100 ml) in the fasting subjects and the difference was highly significant ($P<0{\cdot}001$).

①



②

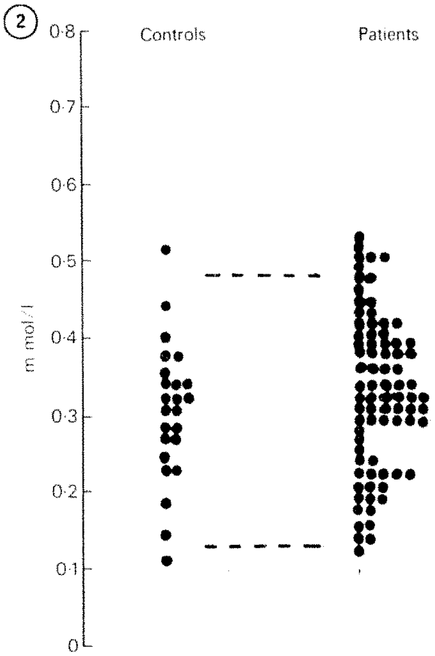


Fig. 1. Plasma concentrations of uric acid in non-fasting and fasting normal men. The horizontal lines denote the mean ± 1 S.E.

Fig. 2. Plasma concentrations of uric acid in fasting normal men and male patients with calcium-containing stones. The dotted lines indicate the normal range (2 SD).

Plasma Uric Acid Levels in Fasting Normal Subjects and Stone-Formers

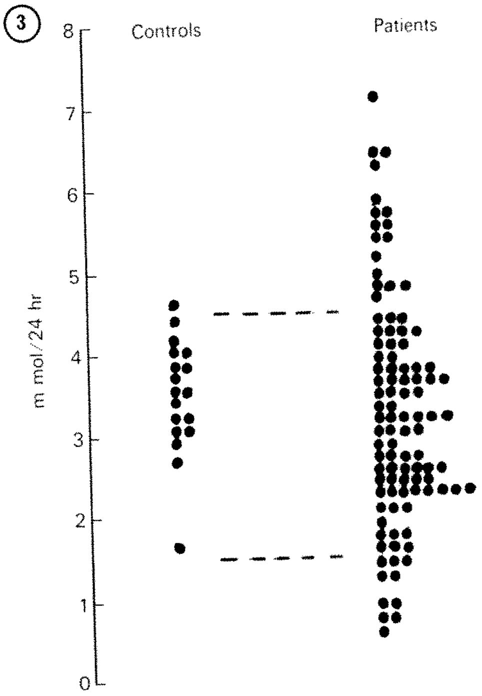
Figure 2 shows the fasting plasma uric levels in 24 normal men and 80 patients. The mean value for the patients (0·33 mmol/l or 5·5 mg/100 ml) did not differ significantly from the mean value for the controls (0·31 mmol/l or 5·2 mg/100 ml). The normal range for 2 standard deviations of the mean was 0·13 to 4·8 mmol/l (2·2 to 8·0 mg/100 ml). 6 patients (7·5%) had values which slightly exceeded the upper limit of this range; repeated measurements on these patients indicated that hyperuricaemia was generally intermittent in nature.

Urinary Excretion

Figure 3 shows the daily excretion of uric acid by the control subjects and stone-formers when on their normal home diet. Excretion by the normal subjects was within the generally accepted normal range of 1·5 to 4·5 mmol/24 hour (250 to 750 mg/24 hour) (Henry *et al.*, 1974), except in 1 case. The mean value for the stone-formers (3·26 mmol or 547 mg/24 hour) did not differ significantly from that of the controls (3·52 mmol or 590 mg/24 hour). 17 patients (17%) had uric acid values which exceeded the normal range, as defined above; repeated measurements on these patients indicated that hyperuricosuria, like hyperuricaemia, was generally intermittent.

Effect of Fasting on the Urine Uric Acid/Creatinine Ratio

The possibility that some of the high urine uric acid values were due to high purine intakes was examined by measuring the uric acid/creatinine ratios in subjects who had fasted overnight. Fasting resulted in a statistically significant fall in the mean uric acid/creatinine ratio in both normal subjects and patients. In 18 controls the mean value fell from 0·233 to 0·153 ($P<0·01$) while in 60 patients it decreased from 0·226 to 0·159 ($P<0·001$).

③


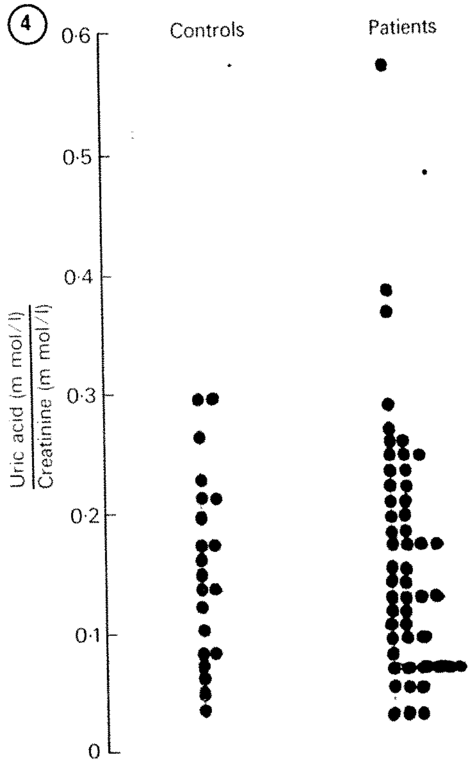
④


Fig. 3. Daily excretion of uric acid by normal men and male patients with calcium stones on normal home diet. The dotted lines indicate the generally-accepted normal range (Henry *et al.*, 1974).

Fig. 4. Ratios of uric acid to creatinine (m.mol/l) in urine of normal men and male patients with calcium stones, after fasting overnight.

Only 1 out of 51 patients (2%) had an unequivocally raised uric acid/creatinine ratio when fasting (Fig. 4), indicating that most of the high urine uric acid values were dietary in origin.

Relation between Uric Acid Excretion and other Urine Parameters

The daily excretion of uric acid by 100 patients was compared with the excretion of creatinine, calcium, phosphate and oxalate by the same subjects. No significant relationship was found between uric acid and creatinine or calcium excretion but there was a moderate correlation between uric acid and phosphate and a highly significant relationship between uric acid and oxalic acid excretion (Table).

Further examination of the data revealed that uric acid and oxalic acid excretion were closely correlated with urine volume, whereas creatinine, calcium and phosphate excretion were not (Table). The significance of these results is discussed below.

Discussion

The present study has not confirmed the rather high incidence of hyperuricaemia and/or hyperuricosuria in patients with calcium-containing stones which has been reported in some surveys (Smith *et al.*, 1969; Dent and Sutor, 1971; Coe and Cavalach, 1974). As far as the plasma is concerned, this may be due to the fact that we examined only fasting blood samples whereas

Table

Relation of Uric Acid Excretion to other Urine Parameters

Parameters (m.mol or ml/24 h)	Number of samples	Correlation coefficient (r)	Probability (p)
Uric acid/creatinine	100	0·074	n.s.
Uric acid/calcium	100	0·162	n.s.
Uric acid/phosphate	100	0·283	<0·01
Uric acid/oxalic acid	99	0·414	<0·001
Creatinine/urine volume	100	0·077	n.s.
Calcium/urine volume	100	0·075	n.s.
Phosphate/urine volume	100	0·076	n.s.
Uric acid/urine volume	100	0·521	<0·001
Oxalic acid/urine volume	99	0·541	<0·001

most other workers have examined non-fasting samples. The effect of diet on plasma uric acid is well documented (Brøchner-Mortensen, 1940; Bishop and Talbot, 1953; Nugent and Tyler, 1959) and our own studies have shown that the level in healthy adults may be reduced by more than 0·1 mmol/l (1·6 mg/100 ml) following overnight fasting. However, urine uric acid is probably of greater interest than plasma uric acid from the standpoint of stone formation and, here again, most of the high values appeared to be due to the diet, since they were largely abolished by fasting (Fig. 4).

It appears, therefore, that most of the uric acid abnormalities found in stone-formers may be attributed to an excessive intake of purine-rich foods, a conclusion which has also been reached by Coe and Cavalach (1974) and Hartung and Bergmann (1974). These findings may have some bearing upon recent suggestions that stone incidence is related to living standards, being more common in professional people than in manual workers (Leading article, *British Medical Journal*, 19th June 1971.) Possibly the higher incidence of uric acid abnormalities in the United States and London, compared with Leeds, is due, at least in part, to differences in living standards which, in turn, determine the consumption of purine-rich foods.

The close relationship between uric acid and oxalic acid excretion (Table) appears, at first sight, to indicate a metabolic link between these 2 compounds but the main factor appears to be the influence of urine flow on the excretion of both substances. A direct relationship between oxalic acid excretion and urine flow has been noted previously (Zarembski and Hodgkinson, 1969; Dhar and Kaul, 1973) and a similar relationship has been observed in the case of uric acid, at urine flow rates below about 1 ml/min (Brøchner-Mortensen, 1940).

Summary

Plasma and uric acid levels were measured in 132 men with calcium-containing renal stones and in 24 healthy men of similar ages.

Fasting resulted in a significant fall in the mean plasma uric acid level of normal subjects. Intermittent hyperuricaemia was observed in 7% of fasting patients. Intermittent hyperuricosuria was found in 17% of non-fasting patients but in only 2 to 6% of fasting subjects.

Most of the uric acid abnormalities in patients with calcium stones therefore appear to be due

to diet and may be prevented by reducing the consumption of purine-rich foods. A direct relationship was observed between uric acid excretion and urine flow at normal flow rates.

It is suggested that the apparent increase in stone incidence, which occurs with rising living standards, may be due partly to increased consumption of purine-rich foods.

The author wishes to thank Professor B. E. C. Nordin for his interest and advice in this study and Mrs W. Jakeman and Mrs S. Eames for the calcium, phosphorus and creatinine determinations. The author would also like to thank P. Bisset for his technical assistance.

References

BISHOP, C. and TALBOTT, J. H. (1953). Uric acid: its role in biological processes and the influence upon it of physiological, pathological and pharmacological agents. *Pharmacological Reviews*, **5**, 231-273.

BRØCHNER-MORTENSEN, K. (1940). The uric acid content in blood and urine in health and disease. *Medicine*, **19**, 161-229.

COE, F. L. and CAVALACH, A. G. (1974). Hypercalciuria und hyperuricosuria in patients with calcium nephrolithiasis. *New England Journal of Medicine*, **291**, 1344-1350.

DENT, C. E. and SUTOR, D. J. (1971). Presence or absence of inhibitor of calcium-oxalate crystal growth in urine of normals and of stone-formers. *Lancet*, **2**, 775-778.

DHAR, G. L. and KAUL, S. (1973). Oxalic acid excretion in Kashmiri adults. *Journal of the Indian Medical Association*, **61**, 76-78.

GUTMAN, A. B. and YÜ, T. F. (1968). Uric acid nephrolithiasis. *American Journal of Medicine*, **45**, 756-779.

HARTUNG, R. and BERGMANN, M. (1974). Oxalatlithiasis and hyperurikurie. *Helvetica Chirurgica Acta*, **41**, 405-410.

HENRY, R. J., CANNON, D. C. and WINKELMAN, J. W. (1974). Clinical chemistry: principles and technics. 2nd ed. New York: Harper, p. 534.

HODGKINSON, A. (1971). A combined qualitative and quantitative procedure for the chemical analysis of urinary calculi. *Journal of Clinical Pathology*, **24**, 147-151.

HODGKINSON, A. and WILLIAMS, A. (1972). An improved colorimetric procedure for urine oxalate. *Clinica Chimica Acta*, **36**, 127-132.

MAYER, G. G., CHASE, T., FARVAR, B., WAIDH, M. A., LONGO, F., KARP, F. and ZINSSER, H. H. (1968). Metabolic studies on the formation of calcium oxalate stones, with special emphasis on vitamin B_6 and uric acid metabolism. *Bulletin of the New York Academy of Medicine*, **44**, 28-44.

MINTZ, D. H., CANARY, J. J., GARREON, G. and KYLE, L. H. (1961). Hyperuricemia in hyperparathyroidism. *New England Journal of Medicine*, **265**, 112-115.

MUGLER, A. (1970). Lithiase oxalique et trouble du métabolisme de l'acide urique. *Journal d'Urologie et Nephrologie*, **76**, 423-434.

NUGENT, C. A. and TYLER, F. H. (1959). The renal excretion of uric acid in patients with gout and in nongouty subjects. *Journal of Clinical Investigation*, **38**, 1890-1898.

ORY, E. M., HISEY, D. P. and REDMOND, D. E. (1970). Acute pancreatitis, hypercalcaemia, hyperuricemia and hypertension secondary to parathyroid adenoma. *Southern Medical Journal*, **63**, 194-197.

PRIEN, E. L. and PRIEN, E. L. (1968). Composition and structure of urinary stone. *American Journal of Medicine*, **45**, 654-672.

ROBERTSON, W. G., PEACOCK, M. and NORDIN, B. E. C. (1971). Calcium oxalate crystalluria and urine saturation in recurrent renal stone-formers. *Clinical Science*, **40**, 365-374.

SCOTT, J. T., DIXON, A. S. J. and BYWATERS, E. G. L. (1964). Association of hyperuricaemia and gout with hyperparathyroidism. *British Medical Journal*, **1**, 1070-1073.

SMITH, M. J. V., HUNT, L. D., KING, J. S. and BOYCE, W. H. (1969). Uricemia and urolithiasis. *Journal of Urology*, **101**, 637-642.

ZAREMBSKI, P. M. and HODGKINSON, A. (1969). Some factors influencing the urinary excretion of oxalic acid in man. *Clinica Chimica Acta*, **25**, 1-10.

The Author

A. Hodgkinson, DSc, FRIC, Assistant Director.

British Journal of Urology (1976), **48**, 6 ©

Short Case Report

Duodenal and Common Bile Duct Obstruction with a Pyelo-duodenal Fistula caused by Renal Calculous Pyonephrosis

An 83-year-old lady presented with a 10-day history of epigastric pain, vomiting and constipation. On examination she was slightly dehydrated and had vague generalised abdominal tenderness with a succussion splash. A diagnosis of pyloric stenosis was made. Initially she was treated conservatively with a satisfactory result.

An X-ray of the abdomen taken on admission showed a staghorn calculus in the right kidney. There was gross distension of the stomach which appeared to extend into and include the first part of the duodenum. A barium meal (Fig.) taken 1 week after admission revealed a very large gastric residue and showed that the stomach and first part of the duodenum were dilated and that the second part of the duodenum was obstructed. There were small pools of barium in the body of the stomach and duodenal bulb and also a third tapered pool of barium demonstrated the obstruction in the second part of the duodenum.

A laparotomy confirmed that the second part of the duodenum was obstructed and that the stomach and first part of the duodenum were grossly distended. The obstructing agent was found to be adhesions between the right renal pelvis and second part of the duodenum. On dividing these adhesions a pyelo-duodenal fistula was opened but this was subsequently closed since excision and repair were thought impractical. The obstruction was by-passed by a retrocolic duodeno-jejunostomy between the proximal jejunum and the first part of the duodenum.

Initially the patient progressed well but 3 weeks following the operation she became jaundiced. Liver function tests revealed an obstructive picture. After several weeks the jaundice started to resolve but the patient's condition gradually deteriorated and she died. An autopsy confirmed that there was a fistulous connection between the renal pelvis and the duodenum and demonstrated that the duodenum and common bile duct were surrounded by dense adhesions which arose from a right perinephric abscess. The immediate cause of death was pulmonary embolus.

Comment

Organic obstruction of the duodenum is rare and the combination of duodenal and common bile duct obstruction caused by renal sepsis and associated with a pyelo-duodenal fistula has not been reported previously. McEwan (1968) reviewed 24 cases of spontaneous pyelo-duodenal fistula in the world literature and discussed aetiology and management. Patients usually present with non-specific gastro-intestinal symptoms which are associated with chronic renal sepsis and also on occasions the flow of urine into the duodenum gives rise to a hyperchloraemic acidosis (Boggs, Blundon and Davis, 1961).

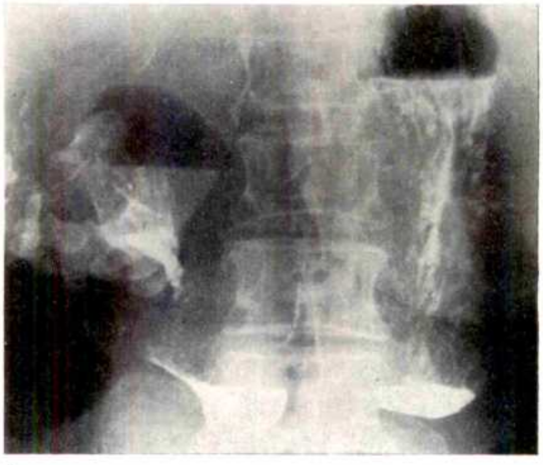
K. P. Boardman
Manchester Royal Infirmary, Manchester M13 9WL

I would like to thank Mr N. C. Keddie, Consultant Surgeon, Manchester Royal Infirmary, for his permission to present this case.

References

Boggs, J. E., Blundon, K. E. and Davis, D. M. (1961). Pyelo-duodenal fistula. *Journal of Urology*, **86**, 199-204.

McEwan A. J. (1968). Pyelo-duodenal fistula. *British Journal of Urology*, **40**, 350-353.



British Journal of Urology (1976), **48**, 7-11 ©

Urinary Citrate Excretion in Stone-Formers and Normal Controls

S. G. WELSHMAN and M. G. MCGEOWN
Departments of Clinical Chemistry and Nephrology, Belfast City Hospital, Belfast

Citrate is a normal constituent of human urine and is known to form a soluble complex with calcium. The physiological implications of this complex formation have been studied by Hastings *et al.* (1934) and by Greenwald (1938). The possibility that a reduction in the urinary excretion of citrate might result in the precipitation of calcium oxalate and the formation of renal calculi has been considered by a number of workers. A reduction in the daily citrate excretions of stone-formers has been reported by Boothby and Adams (1934), Kissin and Locks (1941) and Scott, Huggins and Selman (1943). According to Conway, Maitland and Rennie (1949) only stone-formers with infected urine had a reduced excretion of citrate and they concluded that post-renal destruction of citrate was the probable reason for differences between stone-formers and controls. Hodgkinson (1962) investigated urinary citrate excretion in stone-formers and controls, and concluded that reduced citrate excretion by stone-formers appeared to be the result of impaired renal function. Shorr, Bernheim and Taussky (1942) found that, in women, the excretion of citrate rises during ovulation and that administration of oestrogens increases urinary citrate excretion. In the present study, the 24-hour urinary citrate levels of normal males and females were estimated and compared with those of male and female stone-formers. The results for citrate excretions were also related to urinary calcium excretions.

Material and Methods

24-hour urine collections were obtained from 117 male and 47 female patients with calcium containing stone in whom no aetiological factor had been discovered. These patients were admitted to the Belfast City Hospital over a 3-year period. The diagnosis was established either by the radiological evidence of a stone in the renal tract, or by the passage of a stone or its removal at operation. All patients had normal renal function and were free of urinary tract infection at the time of collection. Stone-formers with such known aetiological factors as hyperparathyroidism, renal tubular acidosis, sarcoidosis and vitamin D intoxication were excluded. Patients with a blood urea over 40 mg/100 ml were excluded from the study.

Patients with frank idiopathic hypercalciuria were included.

There were 2 control groups, patient and non-patient. 24-hour urine collections were obtained from the individuals in each group. 73 male and 85 female patients with various non-renal diseases were used as patient controls and 108 young adults (aged 17-30 years), consisting of army personnel, nurses and laboratory workers, served as non-patient controls. All the female control cases were single; it is not known how many were using an oral contraceptive.

All subjects were on a free diet except that stone-formers were encouraged to maintain a high fluid intake. It was assumed that the effect of individual variations in diet would be insignificant in an investigation involving a relatively large number of persons drawn from a homogeneous population. The difference in diet at home and in hospital ought not to be significant as every attempt is made by this hospital to provide a diet similar to that consumed by the patients at home.

Table I

The 24-hour Urinary Excretion of Citrate (mg/24 hours) of Stone-Formers, Patient Controls and Young Adult Controls

Group		No.	Mean	S.E.M.	S.D.	Actual range
Males	Stone-formers	117	236	16·6	179	12-848
	Patient controls	73	328	30·3	256	12-1232
	Young adult controls	59	370	21·2	172	76-792
Females	Stone-formers	47	221	33·1	201	19-865
	Patient controls	85	344	29·8	275	16-1328
	Young adult controls	49	552	37·7	272	191-1521

Table II

Correlation Coefficients and Linear Regression Equations for Citrate on Calcium in mg/24 hours for Stone-Formers, Patient Controls and Young Adult Controls

Group		No.	Citrate (mg/24 hr)	Calcium (mg/24 hr)	Linear regression equation	*r*	*t* test P
Males	Stone-formers	117	236	203	Cit = 101+0·66 Ca	0·35	<0·01
	Patient controls	73	328	183	Cit = 120+1·14 Ca	0·51	<0·001
	Young adult controls	59	370	213	Cit = 250+0·56 Ca	0·34	<0·001
Females	Stone-formers	47	221	149	Cit = 67+1·07 Ca	0·40	<0·01
	Patient controls	85	344	174	Cit = 239+0·62 Ca	0·26	<0·05
	Young adult controls	49	552	148	Cit = 312+1·63 Ca	0·38	<0·01

Citrate in urine was estimated by a specific method using citrate lyase (Welshman and McCambridge, 1973). Calcium was determined by an autoanalyser technique (Technicon Methodology N-3B), involving the reaction of cresolphthalein complexone with calcium in the presence of diethylamine. Creatinine was determined by the alkaline picrate reaction, using an autoanalyser (Technicon Methodology N-11b).

Results

The mean 24-hour citrate excretion, expressed as mg per 24 hours, of stone-formers, young adult controls and patient controls, are given in Table I. The mean citrate excretion of the male stone-formers was significantly lower ($P<0·01$) than that of the male patient and young adult controls. The female stone-formers also showed a significantly lower citrate excretion ($P<0·01$) as compared with the female patient controls, and a highly significant difference ($P<0·001$) when compared with the young adult female controls.

The mean citrate excretions of the corresponding male and female groups were compared. No significant difference ($P>0·05$) was observed between the male and female stone-formers. There was also no significant difference ($P>0·05$) in citrate excretion between the male and female patient controls. In the young adult control group, females exhibited a highly significant increase ($P<0·001$) in citrate excretion relative to the males.

The urinary citrate excretions of stone-formers and controls were compared with their 24-hour urinary calcium. These values and the linear correlation equations for citrate on calcium are shown in Table II. A significant correlation was observed for citrate on calcium in all groups. Citrate excretion was found to rise with increasing calcium excretion. Using analysis of covariance it was found that the linear regression lines for the male stone-formers and both male control

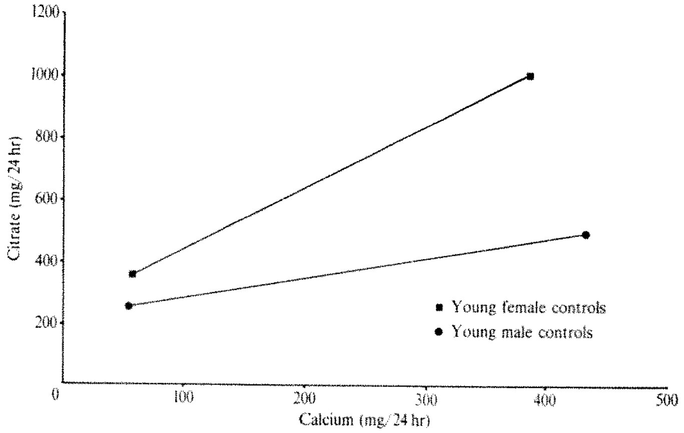


Fig. 1. Linear regression lines of urinary citrate on calcium for young male controls and young female controls.

groups did not differ significantly in either slope or position ($P > 0{\cdot}05$). The linear regression lines for female stone-formers and both female control groups were not significantly different in slope ($P > 0{\cdot}05$). However the positions of the lines for the young adult females and the female stone-formers are significantly different ($P < 0{\cdot}05$) showing that the mean citrate excretion relative to calcium is greater in the young female controls compared with the female stone-formers.

The linear regression equations of citrate on calcium for the young adult male and female controls given in Figure 1, are significantly different in slope ($P < 0{\cdot}001$), indicating that the young females excrete significantly more citrate than the young male controls as the calcium excretion rises.

The mean citrate excretion for stone-formers, patient controls and young adult controls were also calculated in mg per gram of creatinine. In Table III the results were compared with the urinary calcium results in mg per gram of creatinine. The linear regression equations for citrate on calcium and the correlation coefficients are also given in Table III. These results confirm the findings already expressed in mg per 24 hours. The young adult female controls showed a much higher excretion of citrate than males ($P < 0{\cdot}001$), although the calcium excretions relative to creatinine for the males and females were similar. There was a significant linear relationship between calcium and citrate for all groups (Table III). The linear regression equations for all groups, both male and female, were similar with the exception of the young adult female

Table III

Correlation Coefficients and Linear Regression Equations for Citrate on Calcium in mg per gram of Creatinine for Stone-Formers, Patient Controls and Young Adult Controls

	Group	No.	Citrate (mg/1 g Creat.)	Calcium (mg/1 g Creat.)	Linear regression equation	*r*	*t* test P
Males	Stone-formers	94	182	155	Cit = 85+0·63 Ca	0·33	<0·001
	Patient controls	72	236	135	Cit = 124+0·83 Ca	0·37	<0·001
	Young adult controls	55	266	150	Cit = 214+0·35 Ca	0·26	<0·05
Females	Stone-formers	41	202	128	Cit = 101+0·79 Ca	0·31	<0·05
	Patient controls	85	345	177	Cit = 262+0·47 Ca	0·21	<0·05
	Young adult controls	49	581	161	Cit = 305+1·71 Ca	0·46	<0·001

controls. This group had a significantly different slope ($P<0{\cdot}001$), indicating a greater increase of citrate excretion relative to calcium.

Discussion

The normal mean values obtained for urinary citrate excretion were lower than those reported by earlier workers (Kissin and Locks, 1941; Conway *et al.*, 1949; Hodgkinson, 1962; Modlin, 1967), probably because a more accurate and specific citrate lyase technique was used for the estimation of citrate.

The marked increase in citrate excretion by healthy young females as compared with males, observed in this investigation, has also been reported by Hodgkinson (1962). The sex difference in citrate excretion is probably the result of the opposing effects of androgenic and oestrogenic hormones on the excretion of citrate in urine. Shorr *et al.* (1942) have noted a rise in citrate excretion in women during ovulation and after the administration of oestrogens to males and females. These workers also found a decrease in citrate excretion when testosterone was administered to male and female subjects. It was observed in this study that patient controls did not show any significant difference in urinary citrate excretion between the sexes. As most of these patient controls belonged to an older and mostly post-menopausal group (40-70 years), the reduction of their daily citrate excretion to the level of the males was probably related to a reduced output of oestrogenic hormones.

The daily excretion of urinary citrate was found to be significantly reduced in both male and female stone-formers. This phenomenon has been observed by other investigators (Kissin and Locks, 1941; Scott *et al.*, 1943). However, Conway *et al.* (1949) found that only stone-formers with infected urines exhibited a reduced citrate excretion and that urinary citrate was normal in those patients with sterile urines. Although it is well established that certain commonly occurring organisms, *e.g.* coliforms, do destroy citrate in urine, Hodgkinson (1962) did not observe any significant difference in urinary citrate excretion between sterile and infected urines. In the present investigation, all stone-formers and controls were examined for urinary tract infection and urines showing bacterial growth on culture were excluded from the investigation; therefore the reduced excretion of citrate shown by the stone-formers was not the result of bacterial action. Hodgkinson (1962) also suggested that reduced citrate excretion by stone-formers was probably the result of impaired renal function. However, patients with renal impairment were deliberately excluded from the study. There is, at present, no obvious explanation for the reduced excretion of citrate by stone-formers but it is clearly not the result of infection or renal insufficiency.

A direct relationship between the urinary excretion of calcium and citrate has been reported by Shorr *et al.* (1942) and Milne (1953). On the other hand, Hodgkinson (1962) did not observe any such definite relationship in the majority of his patients. In the present investigation a significant linear relationship between citrate and calcium was found in all groups studied. The highly significant difference in the slopes of linear regression lines of citrate on calcium for young normal females compared with the corresponding male group, suggest that young women excrete much larger amounts of citrate than young men as calcium excretion rises. In the stone-former and patient control groups the relative excretion of citrate to calcium was not significantly different due to the reduced excretion of citrate by the relatively older females in these 2 groups.

The observed effects of age and sex on citrate excretion appear to coincide with their influence on the incidence of renal stone formation. According to Sutor, Wooley and Illingworth (1974), young males have a significantly higher incidence of kidney stones than females; but in older age-groups, there is no significant difference between males and females. It would seem reasonable that the increased potential for stone formation in young males may well be due to their lower citrate excretion and higher calcium excretion, relative to females and the low level of citrate excretion by stone-formers supports this view.

Summary

A specific method was used for the estimation of citrate in 24-hour urine collections from 108 young adult controls, 158 patient controls and 164 stone-formers.

Stone-formers excreted significantly less citrate in 24 hours than either patient controls or young adult controls.

Stone-formers had a lower concentration of citrate in their urine than either of the control groups.

The young adult females exhibited a much greater excretion of citrate relative to calcium than the young males.

Because of the ability of citrate to complex with calcium ions and keep them in solution, the relatively low incidence of calcium-containing stones in females under 50 years of age could well be the result of their high excretion of citrate and their increased excretion of this substance relative to calcium.

References

BOOTHBY, W. M. and ADAMS, M. (1934). The occurrence of citric acid in urine and body fluids. *American Journal of Physiology*, **107**, 471-479.

CONWAY, N. S., MAITLAND, A. I. L. and RENNIE, J. B. (1949). The urinary citrate excretion in patients with renal calculi. *British Journal of Urology*, **21**, 30-38.

GREENWALD, I. (1938). The dissociation of some calcium salts. *Journal of Biological Chemistry*, **124**, 437-452.

HASTINGS, A. B., MCLEAN, F. C., EICHELBERGER, L., HALL, J. L. and DA COSTA, E. (1934). The ionization of calcium, magnesium and strontium citrates. *Journal of Biological Chemistry*, **107**, 351-370.

HODGKINSON, A. (1962). Citric acid excretion in normal adults and in patients with renal calculus. *Clinical Science*, **23**, 203-212.

KISSIN, B. and LOCKS, M. O. (1941). Urinary citrates in calcium urolithiasis. *Proceedings of the Society for Experimental Biology and Medicine*, **46**, 216-218.

MILNE, M. D. (1953). Urinary excretion of citrate. *Lancet*, **ii**, 731-732.

MODLIN, M. (1967). The aetiology of renal stone: a new concept arising from studies on a stone-free population. *Annals of the Royal College of Surgeons*, **40**, 155-177.

SCOTT, W. W., HUGGINS, C. and SELMAN, B. C. (1943). Metabolism of citric acid in urolithiasis. *Journal of Urology*, **50**, 202-209.

SHORR, E. (1945). The possible usefulness of estrogens and aluminum hydroxide gels in the management of renal stone. *Journal of Urology*, **53**, 507-520.

SHORR, E., ALMY, T. P., SLOAN, M. H., TAUSSKY, H. and TOSCANI, V. (1942). The relation between the urinary excretion of citric acid and calcium; its implications for urinary calcium stone formation. *Science*, **96**, 587-588.

SHORR, E., BERNHEIM, A. R. and TAUSSKY, H. (1942). The relation of urinary citric acid excretion to the menstrual cycle and the steroidal reproductive hormones. *Science*, **95**, 606-607.

SUTOR, D. J., WOOLEY, S. E. and ILLINGWORTH, J. J. (1974). Some aspects of the adult urinary stone problem in Great Britain and Northern Ireland. *British Journal of Urology*, **46**, 275-288.

WELSHMAN, S. G. and MCCAMBRIDGE, H. (1973). The estimation of citrate in serum and urine using a citrate lyase technique. *Clinica Chimica Acta*, **46**, 243-246.

The Authors

S. G. Welshman, PhD, FRIC, Chief Clinical Biochemist.
M. G. McGeown, MD, PhD, FRCPE, Consultant Nephrologist.

British Journal of Urology (1976), **48**, 12 ©

Short Case Report

Complete Avulsion of the Renal Pedicle due to Blunt Injury to Abdomen

Case Report

Mrs D. D. age 53, laundry worker, was brought to the Gravesend Hospital on 1st August 1973 with a crush injury to her abdomen, after being trapped between a clothes press and some railings. On admission she was severely shocked. Her abdomen was tender with generalised rigidity. Intra-abdominal injury was diagnosed. She was taken straight to the operating theatre and resuscitated by giving intravenous plasma followed by blood. Her abdomen was opened under local anaesthetic because of her poor condition. The peritoneal cavity was full of clots. There was no damage to the liver. A second intravenous blood drip was started, the patient was further transfused until it was possible to induce general anaesthesia. A further exploration showed that the right kidney was completely avulsed from its pedicle, the renal vein having torn out of the inferior vena cava and the torn renal artery having retracted behind the vena cava. The kidney was completely blue except for a small area at the lower pole where it was connected by a small lower polar artery supplying an area about ¾″ wide. Presence of left kidney was confirmed by palpation. The right kidney was rapidly removed. An arterial clamp was put longitudinally and the hole in the inferior vena cava was repaired and as a separate ligation of the right renal artery was not possible, it was oversewn with the vena caval wall. Further exploration of the abdomen showed only a small tear in the mesentery and a small tear of the spleen which was oozing. The patient was unfit for splenectomy, the tear was cauterised and sealed with sterispon. The peritoneal cavity was cleared of clots and the abdomen was closed in layers. Postoperatively she was put on ampicillin. She made an excellent postoperative recovery. Urinary excretion was normal. Postoperative X-ray of her dorsi-lumbar spine showed no fracture. She was discharged home on 22nd August 1973.

Since her avulsed right renal artery was included in the suture line of the inferior vena cava, her general practitioner was warned about the remote possibility of developing arteriovenous fistula presenting with the signs of high output failure.

She was seen in the clinic on 19th September 1973 and 21st January 1974 and was very well.

D. G. Jenkins and K. G. Gupta
Gravesend and North Kent Hospital, Gravesend, Kent DA11 0DG

British Journal of Urology (1976), **48**, 13-17 ©

The Elastic Component of Normal and Dilated Ureters in Children: Chemical and Histochemical Characterisation

F. PAGANO, G. PASSERINI, R. CORTIVO, D. DAGA-GORDINI and G. ABATANGELO
Istituto di Istologia ed Embriologia Generale and Department of Urology Università di Padova, Italy

It is generally accepted that congenital urethral valves and other conditions of vesical obstructions are the most frequent causes of dilatation and tortuosity of ureters in children.

Quantitative and qualitative histological studies of the muscle and connective tissue components have been performed by several authors both in normal and dilated ureters (Boone and Smith, 1955; Stein and Weinberg, 1962; Cussen, 1967).

In the normal ureters of the children, the elastic tissue had not been fully investigated and in some cases the investigators were unable to find any elastic fibre, on histological examination (Gill and Emery, 1974).

It is conceivable, however, though the results are not conclusive, that the elastic tissue must play some role in the elasticity of the ureter, which in fact acts as a biological elastometer (Boone and Smith, 1955).

As far as the abnormal ureters in children are concerned, Emery and Gill (1974) have classified the ureters into 5 main classes, ranging from apparently normal (class A) to tortuous and dilated ureters (classes D and E).

Using this histological technique, the authors observed an increase in connective tissue components. The elastic fibres, however, have not been quantitatively estimated, due to the variability of the staining properties of the very fine elastic fibres. The histological observations in these cases represent a limitation for the resolution of this problem.

For this reason we thought it worthwhile to determine the elastin content in both normal and dilated ureters using the chemical extraction procedure which could allow the purification and the chemical analysis of the extracted material.

Materials and Methods

The normal ureters were taken at autopsy from children (age 1-6 years).

The abnormal material pieces were taken during the operation performed on tortuous and dilated ureters of children (age 1-4 years).

The 1 cm segment of each specimen was used for the histological study using the Van-Gieson, haematoxylin and eosin, Weigert's resorcin-fuchsin stainings. In addition, the elastic fibres were also stained with the Sawicki reagent (MBTH, 3-Methyl-2-Benzothiazolone Hydrazone) in order to detect the aldehyde radicals at the level of the elastic tissue (Sawicki *et al.*, 1961; Miller and Fullmer, 1966; Nakao and Angrist, 1968; Abatangelo, Daga-Gordini and Giordano, 1972).

The chemical purification of the elastic tissue was achieved with the autoclave method (Abatangelo *et al.*, 1972).

Some of the autoclaved elastin was further purified with NaOH 0·1 N at 98°C for 45 minutes in order to remove the glycoprotein moiety still present (Gotte and Serafini-Fracassini, 1963; Ross and Bornestein, 1970; Gotte, Mammi and Pezzin, 1972).

The amino acid analyses of the samples were performed after acid hydrolysis in 6 N HCl at 110°C for 22 hours, using an amino acid analyser JLC 5AH.

The exose were determined with the anthrone method (Scott and Melvin, 1953).

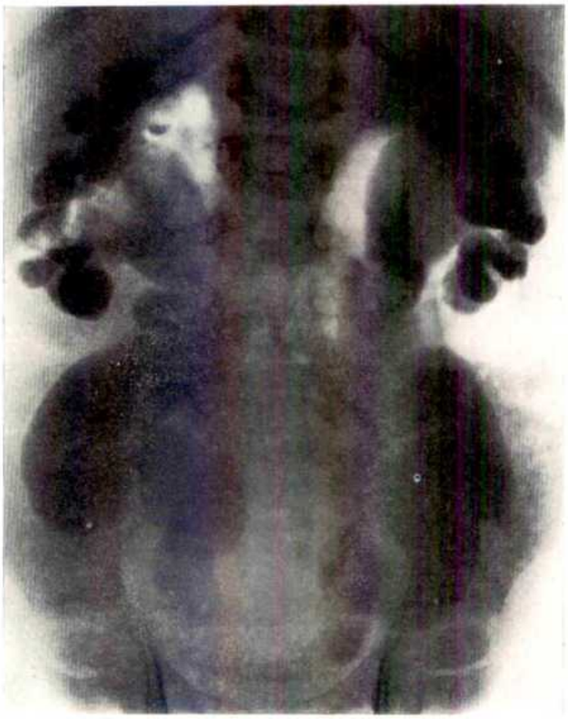


Fig. 1. Intravenous pyelogram of 4-year-old boy with extremely dilated upper urinary tract secondary to urethral valves.

Results

From the measurements of the wall thickness and from the anatomical aspect, the ureters we investigated can be included in group D of the classification proposed by Emery and Gill (1974) in their recent study. The radiological aspect of 1 of these cases is reported in Figure 1.

As far as the histological structure is concerned, it can be clearly seen in Figure 2 that the elastic tissue is well represented both in the muscle area and in the adventitia. It is also evident that the elastic fibres are in intimate association with the muscle elements, sometimes penetrating even around a single fibre (see Fig. 2).

The quantitative estimation of the elastic tissue has been obtained by extracting the elastin with the autoclave method. By this procedure it is possible to remove all the tissue components, which in fact are solubilised during the various chemical treatments, except the elastin which remains as the only insoluble residue. In this way it has been found that the elastin content in the normal ureter is less than 1% of the organic matrix, while in the abnormal ureters the elastic component varies from 3% to 5%.

The amino acid analysis of the material reveals no significant differences as compared with the elastin obtained from child aortas (see Table). Only tyrosine is significantly decreased when compared with aorta elastin.

Table I also gives results of the amino acid analysis of elastin purified with hot alkali treatment as described in "Methods". As known, this treatment allows the solubilisation of the glycoprotein component which is in intimate association with the elastin (Gotte and Serafini-Fracassini, 1965; Ross and Bornstein, 1970). The removal of this moiety, which represents 5% of the total elastin, is clearly evident from the decrease of polar amino acids.

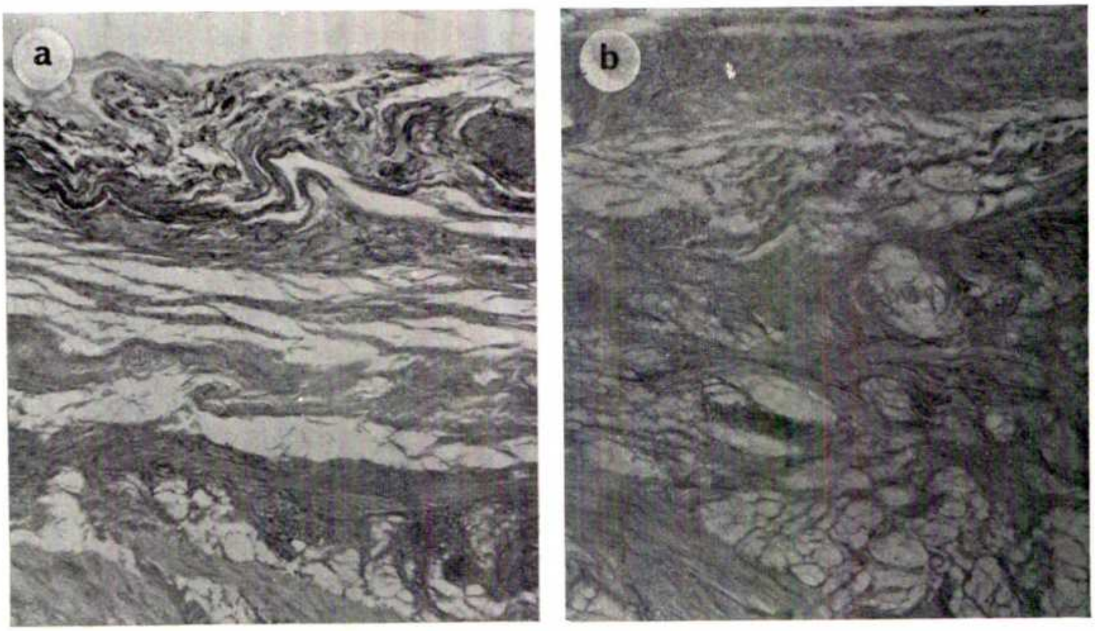


Fig. 2. (a) Surgical specimen of dilated ureter. Note the abundance of elastic tissue in the adventitia and muscle layer. Muscle appears hypertrophied. (Elastin stain, × 100.) (b) The hypertrophied muscle cells are delimited by very thin elastic fibres. (Elastin stain, × 220.)

Discussion and Conclusion

From the histological investigations above reported, it is clearly demonstrated that in the dilated ureteral wall there is a significant increase in connective tissue elements and muscle. Of specific interest, however, is the appearance of numerous elastic fibres which are in intimate association with the muscle elements and in the adventitia.

The elastic fibres appear thin and are easily coloured with all the specific histological methods used for elastin. The only difference is represented by the diminished reactivity with the Sawicki reagent which is employed for the histological demonstration of reactive aldehyde groups. The diminished presence of aldehydes could be responsible for the extreme thinness of the elastic fibres in the ureters as compared with other tissues (aorta, ligaments). In fact the reactive aldehyde groups represent the precursors, in elastin and collagen, of the cross-links which in turn are responsible for the fibre formation and thickening.

As far as the quantitative analysis is concerned, with our methods it has been possible to calculate the exact amount of elastin content in both normal and dilated ureters. It has been clearly demonstrated that in the abnormal ureters, the elastin represents 3% to 5% of the organic material while in the normal ureter it is less than 1%. In addition to this quantitative estimation, we have been able to demonstrate, from the amino-acid analyses, that the elastin synthesised in the ureteral wall, under increased pressure conditions, is comparable to the normal elastin present in other organs such as the elastic arteries. This phenomenon, therefore, represents a reactive response of the elements present in the ureteral wall fibroblasts or muscle cells, to the increased internal pressure, similarly to the response of the aortic wall submitted to hypertension (Wolinski, 1970). In addition, the histological organisation of the elastic fibres closely resembles the elastic arteries, in which in fact there is an intimate connection between muscle and elastic fibres already described in the literature (Benninghoff, 1927).

Table

Amino Acid Composition of Purified Elastin obtained of Normal and Abnormal Children's Ureters (Amino Acid Residues per 1,000 Residues)

Amino acid	Abnormal ureters (autoclaved elastin)	Abnormal ureters (NaOH elastin)	Normal ureters (NaOH elastin)	Aorta (NaOH elastin)
OH-Proline	19·7	15·6	13·5	14·3
Aspartic acid	13·9	9·6	11·0	10·0
Threonine	17·9	11·8	12·8	14·6
Serine	14·5	11·0	11·8	12·9
Glutamic acid	33·0	27·0	28·1	24·8
Proline	113·3	120·0	116·9	118·8
Glycine	291·7	294·0	290·6	306·0
Alanine	219·0	230·0	227·0	229·0
Valine	120·7	118·7	122·2	118·7
Isoleucine	27·6	27·4	28·2	25·8
Leucine	65·5	66·7	67·5	66·4
Tyrosine	14·1	14·7	14·6	20·6
Phenylalanine	25·5	27·0	27·5	24·7
Isodesmosine	—	1·45	1·45	1·4
Desmosine	—	3·4	4·3	2·2
Lysine	9·1	8·5	7·8	7·8
Histidine	2·9	3·0	3·5	2·0
Arginine	12·5	9·0	9·6	10·6

In dilated ureters, exposed to an increased hydrostatic pressure, the presence of the elastin may have a functional importance comparable, to some less extent, to that of the elastic vessels. Moreover, this reactive response of the ureteral wall, under such abnormal conditions, is reversible, as demonstrated by clinical observations (Hendren, 1969, 1971*b*; Pagano, Passerini and Rizzoni, 1975). The return to normal function, due mainly to the resumption of myogenic peristalsis, is probably facilitated from the beginning by the presence of the abundant elastic tissue. After this time, the reabsorptive processes appear to be responsible for the resumption of the normal length and size of the ureters; they offer interesting projects for future research.

Summary

Using chemical and histochemical techniques, it has been possible to calculate the exact amount and distribution of the elastin in normal and abnormal ureters in children.

From the quantitative analyses, it has been calculated that in the dilated ureters the elastin content represents the 3% to 5% of the organic material, while in the normal ureters it is less than 1%.

References

Abatangelo, G., Daga-Gordini, D. and Giordano, R. (1972). Histochemical and chemical demonstration of reactive aldehyde groups in elastin. *Journal of Histochemistry and Cytochemistry*, **20**, 1081-1085.

Benninghofp, A. (1927). Ueber die Bezeihungen zwischen elastichem Gerüst und glatter Muskulatur in der Arterienwand und ihre funktionelle Bedeutung. *Zeitschrift für Zellforschung und Mikroskopische Anatomie*, **6**, 348-396.

Boone, A. W. and Smith, A. G. (1955). The elastic properties of normal ureter. *Journal of Urology*, **73**, 481-486.

Cussen, L. J. (1967). Dimensions of the normal ureter in infancy and childhood. *Investigative Urology*, **5**, 164-178.

—— (1967). The structure of the normal human ureter in infancy and childhood. *Investigative Urology*, **5**, 179-194.

EMERY, J. L. and GILL, G. W. (1974). A classification and quantitative histological study of abnormal ureters in children. *British Journal of Urology*, **46**, 69-79.

GILL, G. W. and EMERY, J. L. (1974). The post-natal development of the muscle and connective tissue of the normal ureter. A quantitative study. *British Journal of Urology*, **46**, 81-90.

GOTTE, L., MAMMI, M. and PEZZIN, G. (1972). Scanning electron microscope observations on elastin. *Connective Tissue Research*, **1**, 61-67.

GOTTE, L. and SERAFINI, FRACASSINI, A. (1963). Electron microscope observations on the structure of elastin. *Journal of Atherosclerosis Research*, **3**, 247-251.

HENDREN, W. H. (1969). Operative repair of megaureter in children. *Journal of Urology*, **101**, 491-507.

—— (1971). Recent advances in the management of low urinary obstruction in the newborn. In *Progress in Pediatric Surgery*, vol. 2, ed. P. P. Rickham, Baltimore: University Park Press, pp. 115-145.

MILLER, E. J. and FULLMER, H. M. (1966). Elastin: diminished reactivity with aldehyde reagents in copper deficiency and lathyrism. *Journal of Experimental Medicine*, **123**, 1097-1108.

NAKAO, K. and ANGRIST, A. A. (1968). A histochemical demonstration of aldehyde in elastin. *American Journal of Clinical Pathology*, **49**, 65-67.

PAGANO, F., PASSERINI, G. and RIZZONI, G. F. (1975). Ostruzioni cervico-uretali nella infanzia. Congresso della Societa Italiana di Urologia, Milan.

ROSS, R. and BORNSTEIN, P. (1970). Studies of the components of the elastic fibre. In *Chemistry and Molecular Biology of the Intercellular Matrix*, vol. I, ed. E. Balazs, London: Academic Press, pp. 641-655.

SAWICKI, E., HAUSER, T. R., STANLEY, T. W. and ELBERT, W. (1961). The 3-methyl-2-benzothiazolone hydrazone test. Sensitive new methods for the detection, rapid estimation and determination of aliphatic aldehydes. *Analytical Chemistry*, **33**, 93-96.

SCOTT, T. A. and MELVIN, E. H. (1953). Determination of dextran with anthrone. *Analytical Chemistry*, **25**, 1656-1661.

STEIN, J. and WEINBERG, S. R. (1962). A histologic study of the normal and dilated ureter. *Journal of Urology*, **87**, 33-38.

WOLINSKY, H. (1970). Response of the rat aortic wall to hypertension: importance of comparing absolute amounts of wall components. *Atherosclerosis*, **11**, 251-255.

The Authors

F. Pagano, MD, Professor, Department of Urology.
G. Passerini, MD, Assistant Professor, Department of Urology.
R. Cortivo, MD, Assistant Professor, Department of Histology and Embryology.
D. Daga-Gordini, MD, Assistant Professor, Department of Histology and Embryology.
G. Abatangelo, MD, Professor, Department of Histology and Embryology.

British Journal of Urology (1976), **48**, 18 ©

Short Case Report

Midline Ensheathed Ureters

A 2-year-old boy was investigated for "failure to thrive" and found to have a urinary infection and bilateral hydronephrosis. There was no ureteric reflux and cystoscopic appearances were normal. A ureteric stricture, 2 cms from a normal left pelvi-ureteric junction, was excised.

Exploration on the right side revealed a retrocaval ureter obstructed by the cava just distal to the pelvi-ureteric junction. The vena cava and aorta bifurcated at this level. At a lower level, in the midline, the right and left ureters were ensheathed by a fibrous membrane (Figs. 1 and 2). This sheath was divided, freeing both ureters. The right ureter was divided at the pelvi-ureteric junction, delivered anterior to the vena cava and anastomosed to the renal pelvis. The patient made an uneventful recovery. He remained well and symptom free 2 years later. The function of his left kidney is poor but the right renal function is good.

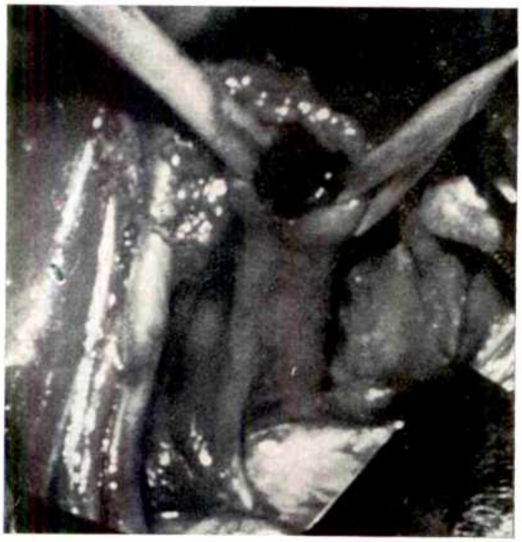


Fig. 1. A photograph showing both ureters (taped superiorly) ensheathed in midline.

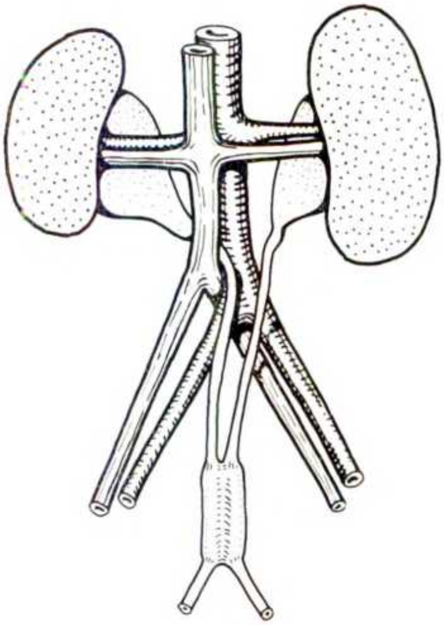


Fig. 2

Comment

Retrocaval ureter is due to persistence of the right postcardinal vein (McClure and Butler, 1925) or the right subcardinal vein (Gruenwald, 1938). In this case the high junction of the iliac veins is probably due to persistence of the postcardinal vein on the right and the supracardinal vein on the left. The sheath may represent vestigial tissue from the embryonic iliac anastomosis.

R. J. SALEM and R. J. LUCK
Department of Surgery, Heatherwood Hospital, Ascot, Berkshire

References

GRUENWALD, P. (1938). Die Genese der Fehlbildungen der Vena Cava caudalis (inferior). *Beitraege zur Pathologischen Anatomie*, **101**, 439-456.

MCCLURE, C. F. W. and BUTLER, E. G. (1925). The development of the vena cava inferior in man. *American Journal of Anatomy*, **35**, 331-384.

British Journal of Urology (1976), **48**, 19–26 ©

Experience with the Ileal Ureter

HESSEIN A. AMIN
Urology Unit, Sabah Hospital, Kuwait

The ileum was first used in urology by Von Mickulicz in 1898 as a means of enlarging the capacity of a contracted bladder. Not until 1950 was attention given to it again, first as an external urinary diversion, then as a replacement of the bladder after cystectomy and only more recently as replacement for ureteric defects.

Houtapel and Grundemann (1960) reported 7 cases which unfortunately were complicated by dilatation. Goodwin and Cockett (1961) succeeded in facilitating the passage of stones in recurrent renal lithiasis by connecting the kidney directly to the bladder with a long loop of ileum. Weinberg (1970) reported his experience in 4 cases of bilharzial ureters treated in Rhodesia by partial ureterectomy and ileal loop replacement. Cordonnier and Bowles (1970) reported 4 cases of successful replacement of ureteric defects by ileum. Uhlíř (1973) reported 1 case of haemangioma of the lower third of the ureter which was resected and successfully replaced by an ileal loop. We present our experience in a series of 18 cases. This started in 1972 when 10 patients were operated upon in rapid succession. They were 10 chronic cases with fistulae, gross hydronephrosis, recurrent infection and sometimes uraemia which had, for long, haunted our wards. The results obtained were a great relief both to patients and to the wards. Table I shows the aetiology and Table II shows whether unilateral or bilateral operation was performed. The clinical presentation is shown in Table III.

Methods

Preoperative gut preparation is essential; oral neomycin is given for 3 days and the gastro-intestinal tract should be empty on the morning of the operation. Cysto-urethroscopy should have been done and any bladder outlet obstruction such as prostatic disease or stricture should have been excluded or treated long before the operation is scheduled. Only if it is a vesical neck contracture can it be dealt with as a part of the operation.

Our routine exposure is a transverse suprapubic Pfannenstiel incision. It offers an excellent exposure of the whole pelvis and the lower halves of ureters, it is extendible lateral to the recti on either side up to the kidney and is rarely followed by incisional hernia. Scars of previous midline exposures are, in our view, a still stronger indication for a transverse exposure, as incisional hernia would otherwise almost certainly follow.

The first step, after a brief intraperitoneal examination, is appendicectomy. The loop is then prepared. Its length depends on the extent of the lesion but 6 inches is a good average. There should be at least one full vascular arch in it with a broad base. Intestinal continuity is restored, the mesenteric gap being always closed transversely and not longitudinally. This keeps the "umbilical cord" of the loop widely based and less liable to torsion. The preparation of the loop should precede the preparation of the ureters, which allows time to detect any possible diminished vascular supply.

The ureters are exposed transperitoneally and it is essential to reach a healthy segment for the anastomosis. If upward intubation shows a higher stricture or if higher ureteric tortuosity *per se* is considered obstructive (Fig. 1) on either side, then the abdominal incision is extended lateral to the rectus on the affected side and the upper lesion is dealt with accordingly. The distal ureter is either ignored, ligated, or resected.

The bladder is then opened, inspected and prepared for the anastomosis. Any vesical neck contracture present is punched out at this stage with our special bladder neck punch (Amin, 1974).

Our usual plans of anastomosis are shown in Figure 2. Thus it will be iso-peristaltic on the left side, and anti-peristaltic on the right side. The left ureter must be passed behind the sigmoid to its right side, so that the anastomosis is not allowed to cross over the colon. If the loop is anastomosed to the lower pole of the kidney it should pass behind and not in front of the descending colon. This was carried out in 1 case in this series (Fig. 3), in whom the left ureter was totally destroyed following repeated ureterolithotomies. The whole loop length was utilised to bridge the gap between the left kidney and bladder. The right ureter had only a single stricture at its lower end and this was dilated and splinted.

Table I

Aetiology

Original pathology	No. of cases
Bilharzial fibrosis of lower third of the ureter	9
Multiple strictures and operations (non-bilharzial)	7
Tuberculosis	2
Irradiation fibrosis	2
Total	18

Table II

Distribution of Sides

Side of operation	No. of cases
Bilateral anastomosis	13
Loop connected to one ureter (other side healthy, 2 cases; other side splinted, 1 case; other side removed, 2 cases)	5
Total	18

Table III

Clinical Presentation

Presentation	No. of cases
Persistent renal fistula (following nephrostomy)	7
Persistent ureteric fistula (following ureterolithotomy or ureterostomy)	6
Palpable painful renal mass	5
Total	18

Table IV

Postoperative Complications

Complication	No.	%
Postoperative mortality	0	0%
Mechanical intestinal obstruction	1	5·5%
Suprapubic urinary fistula (for 6 and 8 weeks only)	2	11%
Minor wound infections	4	22%

A button of bladder tissue should be resected for the ileovesical anastomosis. Theoretically no splint is needed either for the uretero-ileal or for the ileovesical suture-lines. Usually, however, a long Gibbon catheter has been used as a temporary splint on each side. The catheters emerge from the bladder through a separate stab or through the cystotomy incision and are retained for only a few days.

Peritoneal toilet is essential before closure. This consists of abolishing any possible narrow spaces into which gut herniation or strangulation can take place. Sometimes it may be possible to fix the sides of the loop mesentery to the retroperitoneum completely. The flaps of the posterior peritoneal incisions (through which the ureters were exposed) can usually be made to cover the anastomosis itself and obliterate any gaps in the corners. In some cases it is difficult to obliterate a gap and then it is preferable to leave it wide open rather than to narrow it ineffectively.

Results

The immediate convalescence was smooth in most of the cases. Postoperative complications were relatively few and are shown in Table IV. Longer-term results are shown in Table V.

The brighter postoperative clinical picture shown by Table V is usually not equally reflected in the postoperative radiological findings and in spite of the better drainage the dilated, poorly functioning kidneys are not usually much improved.

Mucus is always present mixed with urine in varying degrees. Repeated serum electrolyte estimations, both in hospital and after discharge, have not shown any important derangement attributable to absorption by the ileal loop. Patients are encouraged to increase the fluid intake,

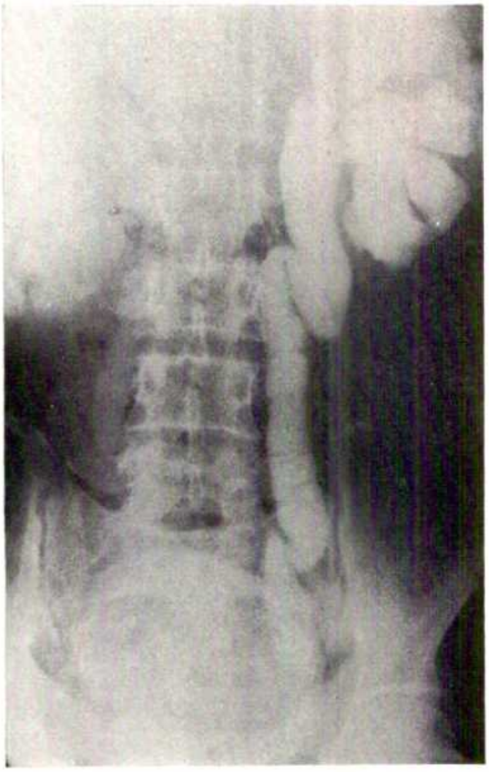


Fig. 1. Such tortuosity *per se* is obstructive, in addition to the distal obstruction.

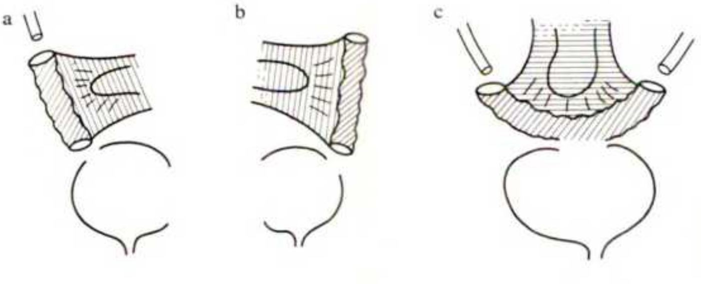


Fig. 2. Usual plans of anastomosis; (a) Right, ureter anastomosis; (b) Left ureter anastomosis; (c) Bilateral anastomosis.

and to micturate at intervals of not more than 2 to 3 hours, even at night. Hiprex (methenamine hippurate) is prescribed as a urinary antiseptic for some weeks or months following the operation, according to the degree of preoperative urinary infection.

The longest follow-up in this series is 3 years (approximately 50% of the cases) and we believe their lives have been made much nearer to normal than before.

Discussion

The use of ileum for the replacement of ureters gives the best alternative at the present time. Boari-Ockerblad vesical flaps can replace only limited defects of the lower segment and that only on one side. Sometimes the flap may even be difficult to fashion in a thickened contracted bladder such as tuberculous or bilharzial. A Boari flap is best applied in unilateral gynaecological injury, with or without ureterovaginal fistula (Amin, 1975).

P25869

Table V

Clinical Results

Presentation	No.	Clinical result	No.
Renal fistula	7	Healed	7
Ureteric fistula	6	Healed	6
Renal mass	5	Size diminished, pain less	3
		Size stationary, recurrent infection, multiple pre-existing stones	2
Total	18	Total	18

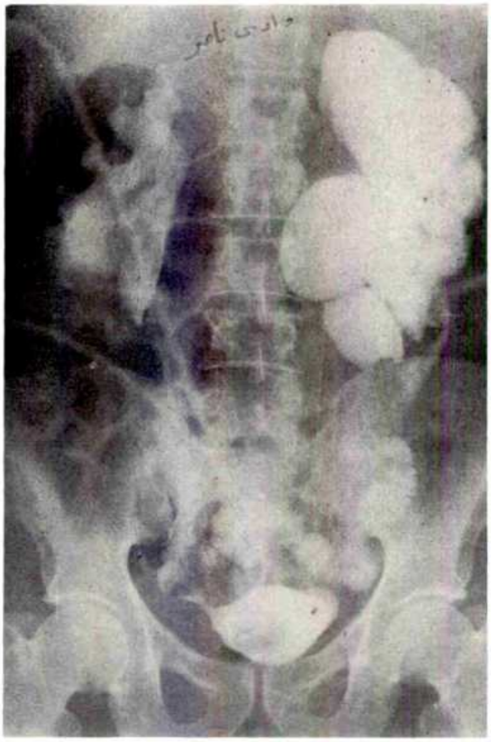


Fig. 3. W. N. age 30, operated 19th August 1972. Stricture lower end right ureter and destroyed left ureter with left nephrostomy fistula. Right ureter was splinted, left ureter was replaced by loop with T-tube at ileorenal anastomosis. Bilateral retrograde X-ray at the time of removal of the right splint; an air bubble noticed in right lower ureter. Patient is now leading a normal active life.

Mucus in the urine has caused very little upset to our patients. It greatly diminishes a few months after operation. Roblejo and Malament (1973) have published a case in which a part of an ileal loop used for ileocystoplasty was resected 12 years later and was subjected to pathological examination. There was marked atrophy of the mucosa and a diminished number of mucoid cells, which shows a change of both the absorptive and mucus secreting characters of the loop lining when it is transferred from the gastro-intestinal into the urinary tract.

The risk of the surgical tailoring of the loop and reconstruction of the gastro-intestinal tract should be no more than the risks of simple gut resection for any other reason. The main hazard is possible mechanical bowel obstruction by internal herniation behind the mesentery of the isolated loop, or behind the ureteric anastomosis. Küss *et al.* (1970) in a review of 185 cases of

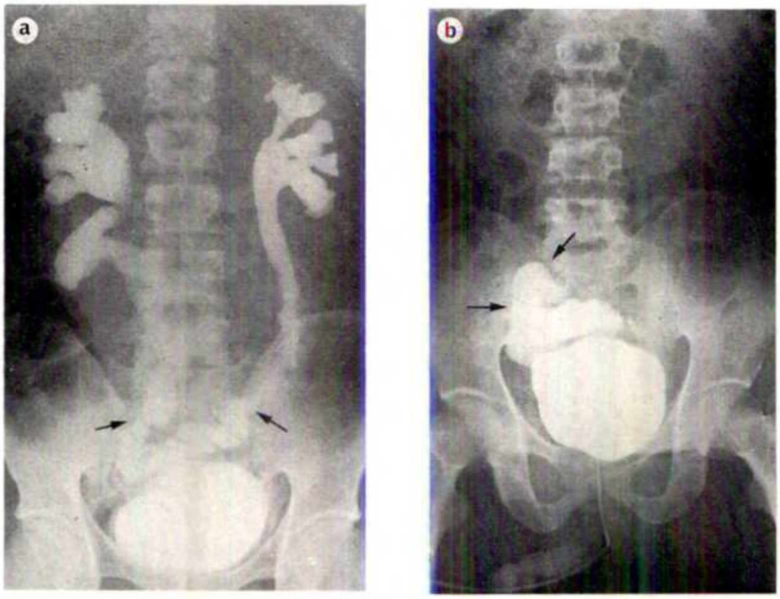


Fig. 4. (a) Retrograde pyelograms of the completed bilateral operation at the time of removal of the tubes; (b) Cystogram a few days later. (Arrows indicate limits of ileal loop.)

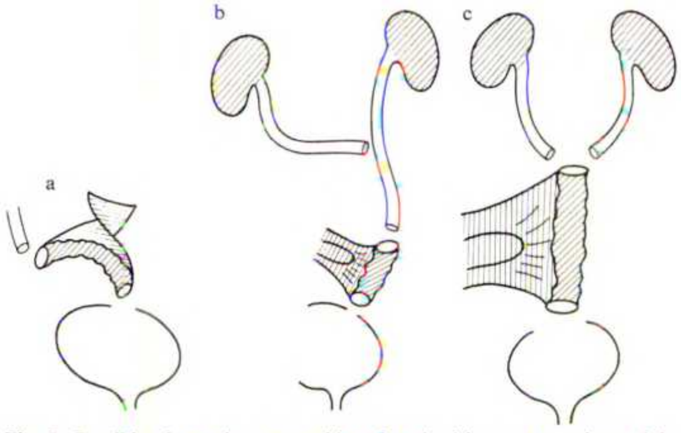


Fig. 5. Possible alternatives to avoid anti-peristaltic anastomosis to right ureter; (a) Twisting of loop; (b) Transureteroureterostomy combined with a short left ureter replacement; (c) Longer loop getting the two ureters at mid-lumbar region, where they are nearest to each other.

sigmoid or ileal loops used for bladder replacement found that mechanical gut obstruction by internal herniation formed the main postoperative complication (11·5%). They warn against non-surgical management of obstruction under the assumption that it may be due to ileus and a low serum potassium; on the contrary they strongly advise early exploration even if the obstruction occurs only a few days following the primary operation. Peritoneal toilet and gap closure is very carefully considered before closure of the peritoneal incision. We had one complication in this respect; the patient was safely relieved by early interference on the 4th postoperative day.

Routine appendicectomy is advised because of possible future hazards to the vascular supply of the isolated loop should appendicitis take place and require operation in another hospital.

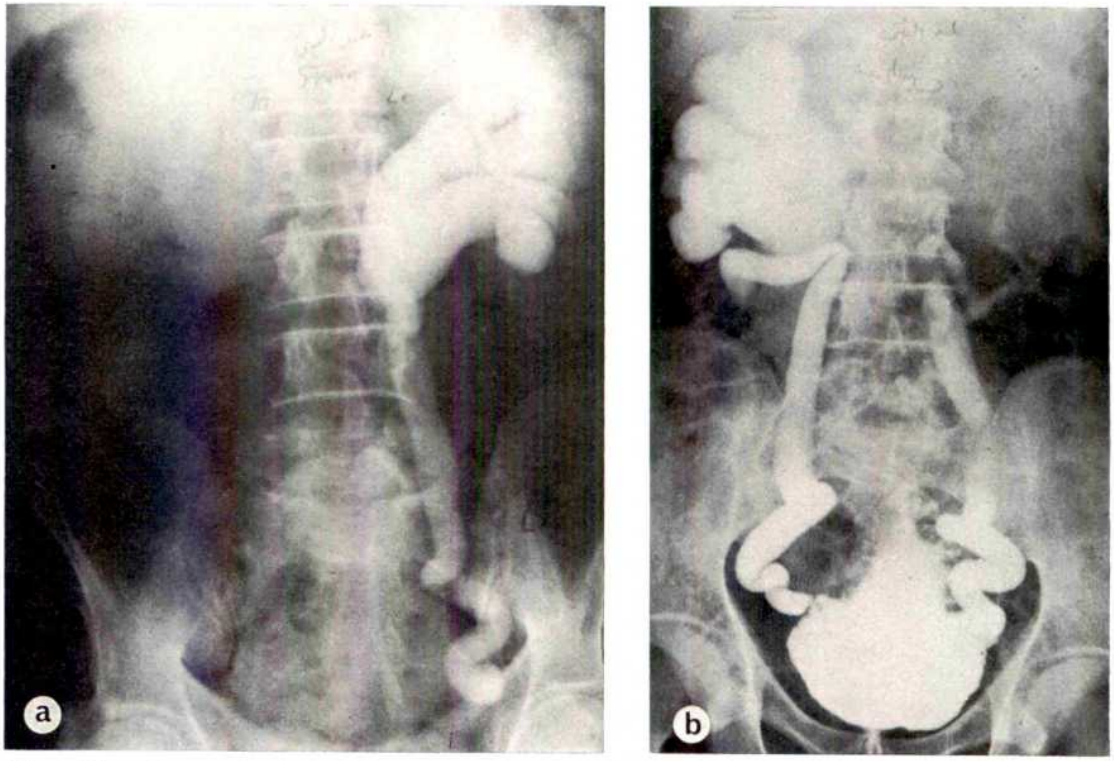


Fig. 6. Bilateral gross ureteric tortuosity caused merely by bladder outlet, obstruction without any ureteric stricture; (a) IVP; (b) Cystogram after TUR.

The patient should know that the appendix has been removed and he should be given a report and diagram of his new anatomy.

Urinary obstruction distal to the loop should be carefully excluded and treated. The 2-layered muscle coat of the loop is much weaker than the 3-layered detrusor and is much more liable to dilate in the presence of distal obstruction. That was the explanation given by Cordonnier and Bowles (1970) for the delayed dilatation of the ileal segment reported in 7 cases by Houtapel and Gründemann (1960). For the same reason we also advise resection of a button of vesical wall at the site of the ileovesical anastomosis, which otherwise may in time become narrowed. This happened in 2 of our earlier cases; both were treated by limited widening of the osteum with cystoscopic scissors.

Reflux has been noticeably absent in left-sided anastomosis but was present in varying degrees on the right side (Fig. 4), probably due to the direction of the loop peristalsis. Shown in Figure 5 are possible alternatives that can secure iso-peristaltic anastomosis. Twisting the loop (Fig. 5a) may positively jeopardise its blood supply (Weinberg, 1970). Transureterostomy (Fig. 5b) or long midline loop (Fig. 5c) both require exposure of the ureters high up in the lumbar region. This may be difficult through the transverse Pfannenstiel incision and may require extending the incision. Oblique or tunnel-like uretero-ileal anastomosis (with a view to preventing reflux) may end in stenosis. We prefer the risk of reflux to the risk of stenosis. Küss *et al.* (1970), in their excellent review of bladder replacement, have shown that reflux when present after, intestino-cystoplasty caused no harm provided there was no distal outlet obstruction.

Reflux *per se*, in the presence of vesical outlet obstruction, can cause much dilatation and tortuosity of the ureters, which could be missed for lower ureteric obstructions. Figure 6 shows

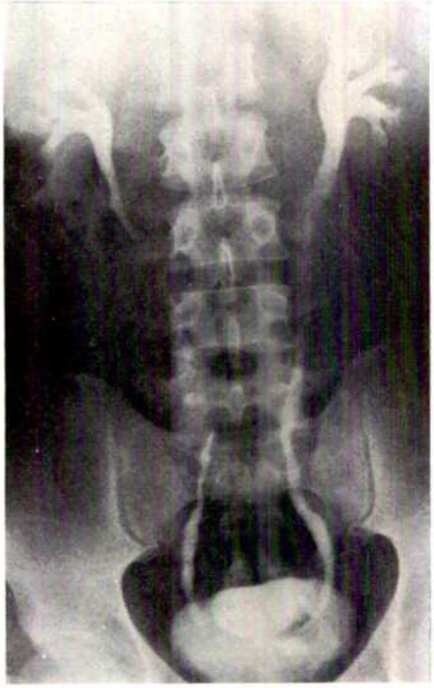


Fig. 7. Acceptable end result of bilharzial ureters, no tortuosity.

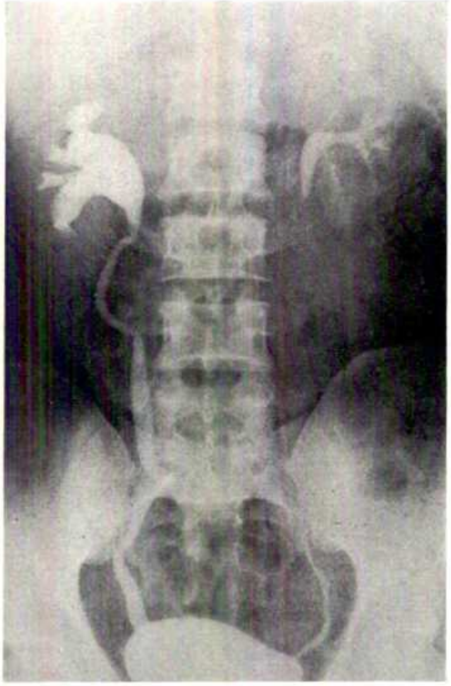


Fig. 8. Early tortuosity caused by stricture; it shows ureteric decompensation and is an indication for interference.

an extreme example of this clinical entity. Transurethral resection of the prostate was all the treatment required.

The lack of much radiological improvement in the IVP is attributed to the long standing structural changes of the kidneys. The earlier these patients are operated upon the healthier are their kidneys. We pass as acceptable many bilharzial-strictured ureters which show mild dilatation, with minimal symptoms, infection or stone formation, as in Figure 7. We accept it to be a reasonable end-result if the patient has migrated from re-infestation areas, has received two ambilhar courses and the IVP remains stationary for 1 year. The appearance of ureteric tortuosity, on the other hand, is a sign of ureteric decompensation. The degree of obstruction in such cases will be progressively deleterious to renal tissue even in the absence of pain, infection or stones; hence the necessity of interference whatever the cause of obstruction. If the lower ureters cannot be repaired then they are better replaced by ileal loop. In Figure 8 we illustrate the optimum time for interference: early tortuosity of the ureter and a well-functioning kidney.

Summary

The isolated ileal loop often provides a satisfactory solution to the problem of extensive ureteric defects. Our experience in 18 cases of diseased ureters partially or totally replaced by isolated ileal loops is presented. The indications for the operation and important operative and preoperative details are discussed.

The operation presents a definite method for renal conservation in many cases in which nephrectomy would otherwise have been unavoidable.

References

AMIN, H. A. (1974). Open resection of the contracted bladder neck. *Journal of the Kuwait Medical Association*, **8**, 19-25.

—— (1975). Uretero-vaginal fistula. *Journal of the Kuwait Medical Association*, **9**, 65-71.

CORDONNIER, J. J. and BOWLES, W. T. (1970). Replacement of ureteral defects by ileal segments. In *Urology*, ed. M. F. Campbell, and J. H. Harrison, 3rd ed. Philadelphia: Saunders, pp. 2296-2299.

GOODWIN, W. E. and COCKETT, A. T. K. (1961). Surgical treatment of multiple, recurrent, branched, renal (staghorn) calculi by pyelo-nephro-ileo-vesical anastomosis. *Journal of Urology*, **85**, 214-222.

HOUTAPEL, H. C. E. M. and GRÜNDEMANN, A. M. (1960). Observations on ileoplasty. *British Journal of Urology*, **32**, 255-266.

KÜSS, R., BIKTER, M., CAMEY, M., CHATELAIN, C. and LASSAU, J. P. (1970). Indications and early and late results of intestinocystoplasty: a review of 185 cases. *Journal of Urology*, **103**, 53-63.

ROBLEJO, P. G. and MALAMENT, M. (1973). Late results of an ileocystoplasty; a 12-year follow-up. *Journal of Urology*, **109**, 38-42.

UHLÍŘ, K. (1973). Hemangioma of the ureter. *Journal of Urology*, **110**, 647-649.

WALLACE, D. M. (1972). Uretero-vaginal fistula. *British Journal of Urology*, **44**, 617-622.

WEINBERG, R. W. (1970). Extensive schistosomiasis of the ureter: the use of the ileal loop in its management. *British Journal of Urology*, **42**, 136-139.

The Author

Hessein A. Amin, MCh, FACS, Head of Urology Unit.

British Journal of Urology (1976), **48**, 27-30 ©

Endometriosis Mimicking Ureterolithiasis

Y. M. TRAUB, J. FISCHELOVITCH, A. NERI and E. LUBIN

Hypertension Unit and Departments of Urology, Gynaecology and Nuclear Medicine, Beilinson Medical Center and Tel Aviv University Medical School, Israel

Ureteral obstruction due to endometriosis is a well-known but quite uncommon finding that has been described more often during the last 15 years (Abeshouse and Abeshouse, 1960; Ball and Platt, 1962; Bates and Beecham, 1969; Stiehm *et al.*, 1972; Yates-Bell *et al.*, 1972; Dick *et al.*, 1973). In a recent review of the literature, Ottolenghi Preti and Parma (1972) were able to collect 76 cases. We here describe a case with unusual clinical and radiological features. We also comment upon the interpretation of various diagnostic procedures that can be used in such cases of partial ureteral obstruction.

Case Report

A 39-year-old nullipara was admitted to the hospital on 16 January, 1974 because of repeated attacks of colicky pain in the right lower abdomen and flank. These attacks started 2 months prior to admission, were unrelated to her menses and increased in severity and frequency during the week preceding hospitalisation. An i.v. urogram performed on 12 December, 1973 and a barium enema had been normal.

The patient's history included essential hypertension, obesity and secondary sterility. She had been followed as an out-patient in our Hypertension Clinic for the last 8 years and underwent extensive workup in 1968, including renin studies and i.v. pyelography which were normal. She has a strong family history of hypertension on the paternal side. Her latest antihypertensive therapy consisted of chlorthalidone, hydrallazine and propranolol. 18 months prior to admission, the patient underwent a right oophorectomy because of a benign cyst of the ovary and excision of a benign fibroma of the uterus.

On admission, physical examination disclosed an obese woman with a blood pressure of 180/110 and no other abnormal findings. On vaginal examination, no abnormality was found. Urinalysis revealed 2-4 erythrocytes per high power field but none was found in a second specimen. Optic fundi and ECG were normal. Routine laboratory studies were within normal limits, except for a serum uric acid concentration of 7·6 mg/100 ml. Serum uric acid had been somewhat elevated occasionally in the past but no special treatment had been felt to be necessary.

An i.v. urogram performed on admission was interpreted as normal but 2 hours later a rapid sequence camera-scintigram using ^{131}I-Hippuran revealed a marked delay in the elimination of tracer-material through the lower portion of the right ureter (Fig. 1). Because of this finding an i.v. urography was repeated 4 days later and again was found to be normal (Fig. 2); the lower ends of the ureters were not clearly visible but this was attributed to the superposition of bony structures.

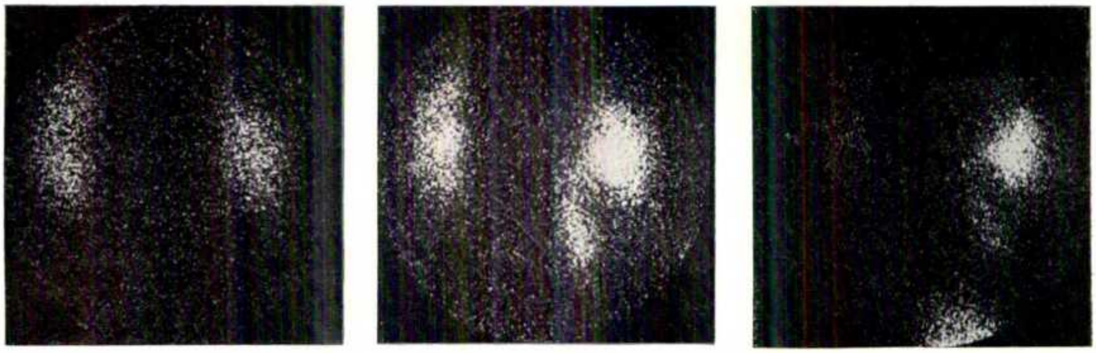


Fig. 1. Rapid sequence camera-scintigram. Pictures taken at 2, 10 and 20 minutes after injection of ^{131} I-Hippuran (16.1.1974).

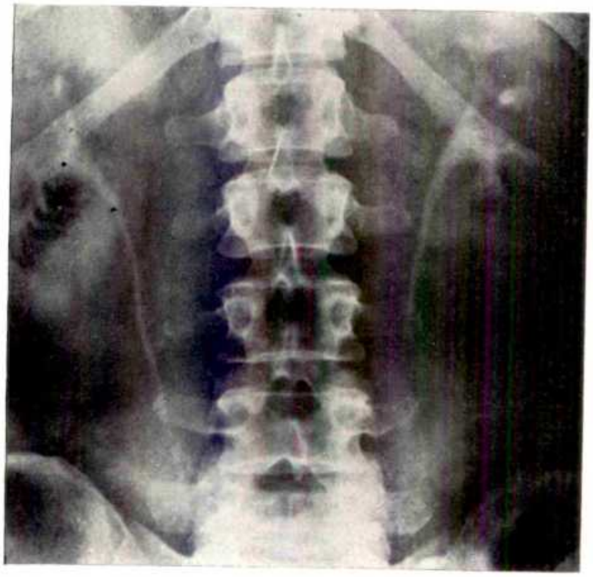


Fig. 2. Intravenous urogram 15 minutes following the injection of contrast material (20.1.1974).

The possibility of a small uric acid stone in the distal portion of the ureter was considered likely and the patient was discharged with a treatment including analgesics and alkalinisation of the urine.

One month later, intermittent attacks of renal colic were still present. A rapid sequence camera-scintigram was very similar to the previous one. At this stage an i.v. drip-infusion urogram was performed and it showed on the right side an incipient hydronephrosis and a 1-cm-wide ureter with a funnel-shaped narrowing of its distal portion (Fig. 3). A retrograde pyelography did not supply any additional information. The patient was again hospitalised and surgical exploration revealed a big multicystic mass apparently originating from the stump of the right fallopian tube surrounding and compressing the lower third of the right ureter. This mass was carefully separated from the ureter and removed. The histologic diagnosis was that of endometriosis.

Following surgery the colicky attacks disappeared. 2 months later an i.v. urogram was normal and 1 year later a rapid sequence camera-scintigram was also normal.

Comment

In a study of 720 cases of endometriosis, Ball and Platt (1962) found 9 cases of endometriosis of the ureteral wall and 4 cases of distortion of the ureter. Endometriosis may cause obstruction of the ureter by invading the ureteral wall, or by affecting the adventitia and surrounding tissues only (Yates-Bell *et al.*, 1972). In our case the ureteral adventitia was infiltrated by the fibrotic tissue surrounding the endometrial cysts.

The clinical picture is usually characterised by abdominal distension, dysmenorrhoea, cystitis, continuous pain in the lower abdomen or flank, or cyclic pain before or during the menstrual period (Berlin *et al.*, 1964; Stiehm *et al.*, 1972; Yates-Bell *et al.*, 1972). Intermittent renal colics, with remissions of a few days' duration and repeatedly normal i.v. urograms over a total period of 4 months is probably a somewhat unusual clinical course.

The fact that the rapid sequence camera-scintigram indicated ureteric obstruction at an early stage, when the i.v. urogram was still interpreted as being normal, illustrates the sensitivity of this test.

Kokkonen, Koskela and Vahala (1971) used radio-isotope renography as a screening procedure and in 19 cases endometriosis was found to be the cause of an abnormal curve. In their paper, however, the authors did not comment on any correlation with i.v. urograms. Although there are problems of correct location of the probes, renogram is undoubtedly a good screening procedure for early detection of uromechanical obstruction but problems of correct location of

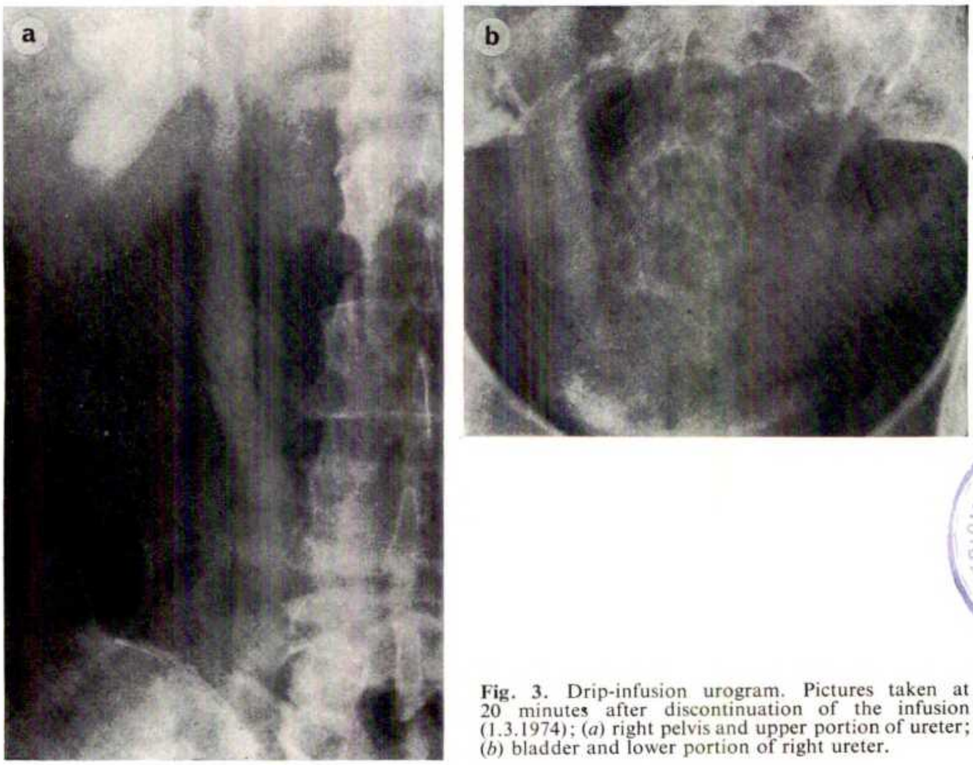


Fig. 3. Drip-infusion urogram. Pictures taken at 20 minutes after discontinuation of the infusion (1.3.1974); (*a*) right pelvis and upper portion of ureter; (*b*) bladder and lower portion of right ureter.

the probes do exist (Meraz and Lubin, 1966). Moreover, the rapid sequence camera-scintigram adds a morphological element in the localisation of the obstruction.

Summary

A case of endometriosis obstructing the right ureter is described, with a clinical picture mimicking ureterolithiasis.

The usefulness of rapid sequence camera-scintigram in the early diagnosis of ureteral obstruction is discussed.

References

Abeshouse, B. S. and Abeshouse, G. (1960). Endometriosis of the urinary tract: a review of the literature and a report of four cases of vesical endometriosis. *Journal of the International College of Surgeons*, **34**, 43-63.

Ball, T. L. and Platt, M. A. (1962). Urological complications of endometriosis. *American Journal of Obstetrics and Gynecology*, **84**, 1516-1521.

Bates, J. S. and Beecham, C. T. (1969). Retroperitoneal endometriosis with ureteral obstruction. *Obstetrics and Gynecology*, **34**, 242-248.

Berlin, L., Waldman, I., White, F. H. and McLain, C. R. (1964). Endometriosis of the ureter. A rare manifestation of a common disease. *American Journal of Roentgenology*, **92**, 351-354.

Dick, A. L., Lang, D. W., Bergman, R. T., Bhatnagar, B. N. S. and Selvaggi, F. P. (1973). Postmenopausal endometriosis with ureteral obstruction. *British Journal of Urology*, **45**, 153-155.

Kokkonen, J., Koskela, O. and Vahala, J. (1971). Benign gynaecological tumours and radioisotope renography. *Acta Obstetricia et Gynecologica Scandinavica*, **50**, 275-278.

MERAZ, D. and LUBIN, E. (1966). The renogram as a method of functional evaluation in the urological patient. *Harefuah*, **71**, 84-88.

OTTOLENGHI PRETI, G. F. and PARMA, A. (1972). L'endometriosi dell'uretere. Presentazione di un caso e rassegra della letteratura. *Annali di Ostetricia Ginecologia Medicina Perinatale*, **93**, 941-955.

YATES-BELL, A. J., MOLLAND, E. A. and PRYOR, J. P. (1972). Endometriosis of the ureter. *British Journal of Urology*, **44**, 58-67.

The Authors

Y. M. Traub, MD, Deputy Head, Hypertension Unit.

J. Fischelovitch, MD, Assistant Director, Department of Urology (now Head, Department of Urology, Emek Hospital, Afula, Israel).

A. Neri, MD, Senior Consultant and Lecturer, Department of Obstetrics and Gynaecology.

E. Lubin, MD, Associate Director and Associate Professor, Department of Nuclear Medicine.

Reprint requests: Dr Y. M. Traub, Hypertension Unit, Beilinson Medical Center, Petach Tikva, Israel.

British Journal of Urology (1976), **48**, 31-37 ©

Re-Implantation of the Ureter[1]

PHILIP CLARK and R. U. HOSMANE

Department of Urology, The General Infirmary and Leeds (St. James's), University Hospital, Leeds

Is the mechanism whereby the ureterovesical junction prevents reflux active or passive? Since Galen in the 2nd century showed that there was no reflux from the bladders of living and dead normal animals and Sir Charles Bell at the beginning of the last century described the muscle fibres of the ureter passing down from the orifice to the bladder neck and prostate, people have been arguing whether the valvular mechanism is active or passive (Bell, 1812; Brock, 1916).

Sampson (1903) was the first person to put forward the case for a passive mechanism forcibly. He thought any intravesical tension would press the anterior lip of the orifice against the posterior ureteric wall, thus occluding the lumen of the ureter. The case for the passive mechanism rests on the fact that the ureterovesical junction of the intact, excised bladder is no less effective and sometimes even more effective, in preventing reflux than it was in the living body.

There is general agreement that in patients with reflux the ureteric orifice is often wider and situated farther from the bladder neck than normal. The submucosal segment of the ureter is therefore shorter than normal. However, Stephens and Lenaghan (1963) observed reflux in infants with duplex ureters, not in the normally sited ureter but in the ureter opening ectopically at the bladder neck. This ureter had a submucosal segment far longer than normal, yet it refluxed. Dissections of the ureterovesical junctions of infants with reflux showed a congenital absence of the submucosal segment, often with wedge-sector defects in the muscle. They postulated that the primary mechanism producing competence is the contraction of Bell's muscle which occludes the ureteric lumen by a "longitudinal shearing action". Tanagho and Hutch (1965) also suggested that the primary cause of reflux was a trigonal muscle deficiency. In addition, Tanagho examined 72 specimens of terminal ureter removed during operations to correct reflux and found that, compared with normal controls, they were deficient in muscle (Tanagho, Guthrie and Lyon, 1969).

The theoretical question, "Is it active or passive?" now becomes a practical one, for, if the lower end of the refluxing ureter is deficient in muscle and the mechanism for preventing reflux is an active one, should not the lower end of the ureter, as Tangaho suggests, be excised?

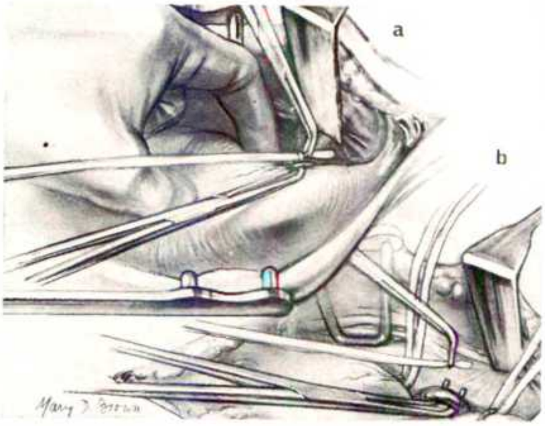
Operative Technique

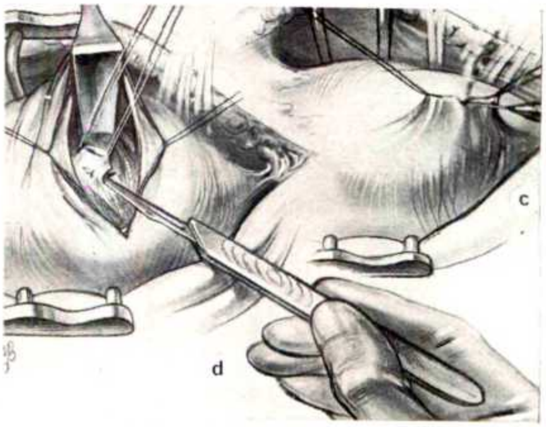
The one thing which all operations to correct reflux have in common is the creation of a long submucosal segment of the ureter. This is achieved with different degrees of mobilisation of the ureter. The most popular operation is that described by Politano and Leadbetter (1958), in which the ureter is completely detached and reintroduced into the bladder through a newly formed, long, submucosal tunnel. For 10 years we have used a modification of this operation.

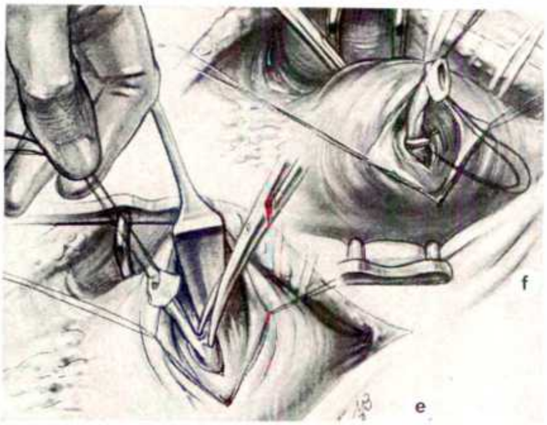
Politano and Leadbetter performed the operation entirely by an intravesical approach but we have always used a combined extravesical and intravesical exposure which has several advantages (Table I). First the ureter is identified extravesically and mobilised from the point where it is crossed by the superior vesical artery to the point where it enters the bladder wall. No arteries need be divided. The bladder is then opened and the ureter is detached in the usual way by intravesical dissection. If there is any difficulty in freeing it at any point deeply, it can be pulled outside the bladder and the final separation can be completed with ease extravesically.

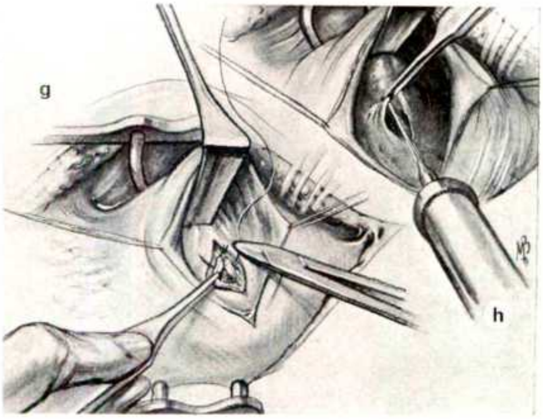
---

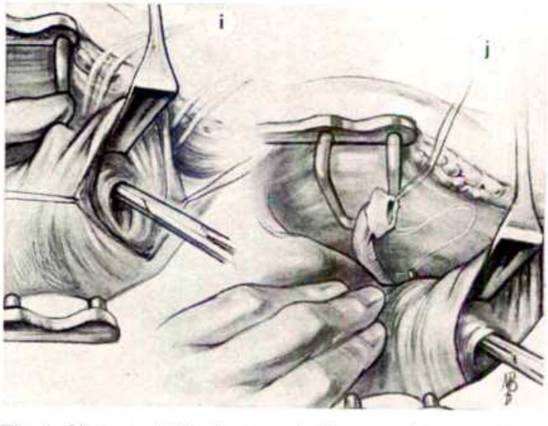
[1] Presented at the 28th Annual Meeting of the Urological Society of Australasia in Sydney, April 1975.











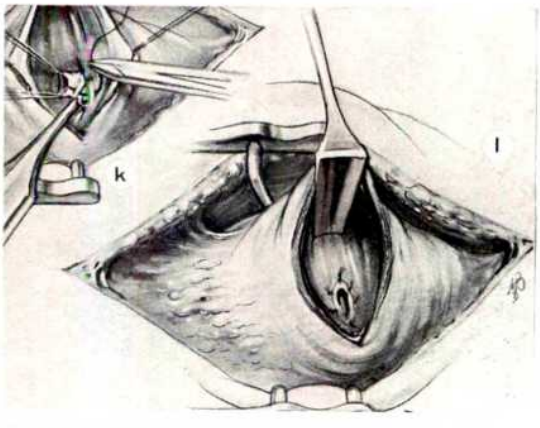


Fig. 1. Ureter mobilised extravesically; one sling passed around superior vesical artery (a), another around ureter (b).
Fig. 2. Bladder opened transversely (c). Mucosa slit to form cuff around ureteric orifice (d).
Fig. 3. Ureter-dissected up intravesically (e); about to be passed extravesically (f).
Fig. 4. Hole in bladder muscle closed (g). Saline injected submucously to facilitate dissection of tunnel (h).
Fig. 5. Angled forceps passed up tunnel and pushed through bladder muscle (i). Ureter about to be passed intravesically (j).
Fig. 6. Ureter sutured back to its original site (k). Final state (l).

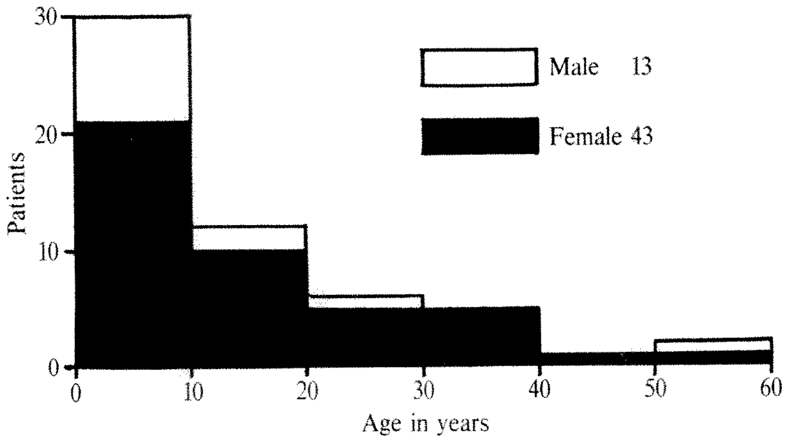


Fig. 7. Histogram showing age and sex of the patients.

Because of the combined exposure, it is unnecessary to incise the bladder mucosa at the upper end of the submucosal tunnel to make the new hole in the bladder muscle. Angled forceps may be passed up the tunnel, turned outwards and pushed through the bladder muscle so that they emerge accurately in line with the ureter and near to the point to which it has been mobilised. The combined exposure ensures that accidental perforation of the peritoneum or even of the intestine, which has been described, does not occur and that when the ureter is drawn back again through the new tunnel and into the bladder it is not angulated or twisted.

Other minor details of this technique are illustrated in Figures 1 to 6. The skin incision is made vertically in the midline. Figure 1a and b shows the ureter being mobilised extravesically. The bladder is opened transversely (Fig. 2c). Two monofilament stay sutures are inserted to elevate the orifice using sutures of different colours to identify the top and bottom end. The circular incision around the orifice is made well away from it and with a fine, straight scalpel by slitting the mucosa outwards (Fig. 2d). The ureter is detached in the normal way (Fig. 3e) and brought extravesically (Fig. 3f). The hole in the bladder muscle is closed with two interrupted stitches (Fig. 4g) and the submucosal tunnel is fashioned after lifting the mucosa off the bladder muscle with a submucous injection of saline (Fig. 4h). Angled forceps are passed up the tunnel, turned outwards and pushed through the bladder muscle in line with the ureter (Fig. 5i). The ureter is then brought back into the bladder (Fig. 5j). The ureteric orifice is only advanced towards the bladder neck if the submucosal tunnel would otherwise be too short. Usually it is sutured back into its original site and the lower stitches in the marked, bottom end of the ureter are made to take a firm bite of the underlying muscle to anchor the ureter and prevent retraction (Fig. 6k). Figure 6l, shows the final state.

The ureter is not splinted. The bladder is drained with a fine, urethral catheter for between 2 and 7 days.

Results

In the last 10 years we have re-implanted 91 ureters in 56 patients by this technique, which preserves the lower end of the ureter, after trying the classical intravesical and Paquin's operation (Paquin, 1959).

13 of these patients were male and 43 female; their ages ranged from 1 to 60 and the majority were under 10 years old but notice that quite a number of adults had re-implantations (Fig. 7).

4 ureters were associated with Hutch diverticula. 4 other ureters were duplex and were treated just like single ureters (and counted as single ureters in the analysis). 12 ureters were advanced

Table I

Advantages of Combined Extravesical/Intravesical Approach

Can finish freeing uterer from bladder extravesically
Upper end of submucosal tunnel left intact
Ureter re-enters bladder wall at correct place externally
No danger of perforating peritoneum or viscus
No danger of angulating or twisting ureter

Table II

Immediate Complications

	Patients
Haematoma of wound	2
Infection of wound	1
Pulmonary embolus	1

Table III

Late Complications

Progressive renal failure	4 patients
Persistent reflux	1 ureter
Obstruction	2 ureters

Table IV

Relief of Symptoms

	Patients	Cured	No change
Urinary infection	39	28	11
Loin pain	24	20	4
Incontinence: day	7	7	—
night	17	10	7

Table V

Advantages of Preserving the Lower End of the Ureter

- Maximum length of ureter preserved
  - no tension on anastomosis
  - no need to mobilise ureter far
  - easy to advance orifice
- Ureteric orifice + cuff preserved
  - stitches away from orifice

towards the bladder neck. There were no grossly dilated ureters in this series and no ureter was tailored or trimmed.

In 3 patients in whom reflux had been demonstrated up only 1 ureter and only that ureter had been re-implanted, reflux occurred up the other ureter postoperatively. Subsequently, because of this, even though reflux had been shown up only 1 ureter, if both ureteric orifices appeared equally gaping and equally displaced laterally, both ureters were re-implanted at the same operation. This was done in 13 patients. In 7 of these patients the intravenous pyelogram showed pyelonephritis or dilatation of the collecting system on both sides suggesting that bilateral reflux occurred.

There was no operative mortality. Postoperative recovery was usually remarkably uneventful (Table II). 2 patients developed a haematoma and 1 an infection of the wound. One patient had a pulmonary embolus but recovered fully. Although the blood-urea level might rise transiently, significant ureteric obstruction did not occur, even though splints were not used.

The average follow-up period of these patients was over 4 years.

4 patients with bilateral pyelonephritis and a raise blood-urea level at the time of their operation had progressive deterioration of renal function in the years following operation and 3 have died, presumably as the result of progressive fibrosis of their kidneys (Table III). Operation was still probably worthwhile in that they had no further urinary symptoms and no further attacks of urinary infection. Altogether, there were 13 patients who had blood-urea levels of over 40 mg per 100 ml (7·1 mmol/l) at the time of their operation; of the other 9 patients, in 3 the level has remained static and in 6 it has returned to normal or near-normal levels. 5 of these 13 patients

were hypertensive at the time of their operation. 2 had progressive deterioration of renal function and died; in 1 the blood-urea level remained static; in 2 it decreased.

One patient, who had leukoplakia involving the ureteric orifice and a urethral stricture requiring repeated dilatation (and was also the oldest patient in the series) has not been cured of reflux by re-implantation. Due perhaps to soft-heartedness, postoperative micturating cystograms were done on only 46 of the other 55 patients (a general anaesthetic would have been needed to catheterise some of the children) but there is no reason to believe reflux is occurring in any of the other 9 patients. This gives a reflux rate of 1 in 76 ureters, or 1 in 64 ureters in which reflux had been demonstrated preoperatively.

2 patients developed obstruction of a ureter and have been treated by re-implanting their obstructed ureter into a Boari flap. In 1 patient the cause of the obstruction was not apparent; in the other the cause was faulty technique, the angled forceps having been inadvertently pushed through a fold of bladder mucosa before perforating the bladder muscle. This resulted in the ureter crossing the lumen of the bladder and being angulated before it entered the submucosal tunnel—a fault which was subsequently easily avoided.

In the other patients the relief of symptoms by the operation was usually dramatic (Table IV). Often the patient would have no further attacks of urinary infection, no further loin pain and would become dry from the day of operation. A child, who before the operation had been listless, irritable and below average weight, would become active and happy and would put on a spurt of growth.

Several patients needed to be on antibiotic therapy for up to 2 months to eradicate urinary infection; 4 patients had 1 or 2 isolated attacks of urinary infection but recurrent attacks continued in only 11 patients; one of these had renal stones and 2 adult patients had urethral strictures requiring repeated dilatation. Loin pain was usually cured, though 4 patients have continued to have occasional twinges of pain. Diurnal incontinence has been cured but nocturnal enuresis persists in 7 out of 17 patients; 2 of these had a Y-V plasty of the bladder neck, an operation which is now generally thought to be rarely indicated.

Pyelograms were usually done on these patients every 2 years after operation. Dilatation of the collecting system sometimes took 1 or 2 years to disappear but unlike the dilatation caused by obstruction which may persist. When the dilatation disappeared, previously unnoticed pyelonephrotic changes sometimes became apparent. The radiological changes of pyelonephritis persisted.

Discussion

Is the mechanism which prevents reflux active or passive? The lower end of the ureter was carefully preserved in all these patients; if it was deficient in muscle as Tanagho suggests, it remained deficient. In the majority the ureteric orifice was carefully replaced in its original site; if the trigonal muscles were weak, they remained weak. Nevertheless, in all but 1 patient reflux was prevented. Reflux can be prevented by this or by any other operative procedure which creates a long submucosal segment of the ureter. The aim should be to restore the passive mechanism which prevents reflux.

How then can we explain the reflux described by Stephens and Lenaghan in ectopic ureters with very long submucosal segments? Figure 8 is the micturating cystogram of a boy with an ectopic duplex ureter ending at the bladder neck in a ureterocele. The actual orifice was very wide and admitted a panendoscope with ease. It would certainly have allowed urine to flow in and out. Is it too far-fetched to imagine that, trapped within the contracting bladder neck during micturition, this ureterocele might have acted like a Higginson's syringe and actually squirted urine up the ureter?

Should the lower end of the ureter be excised? The results presented show that it is unnecessary to excise the lower end of the ureter for possible muscular deficiency or for any of those curious

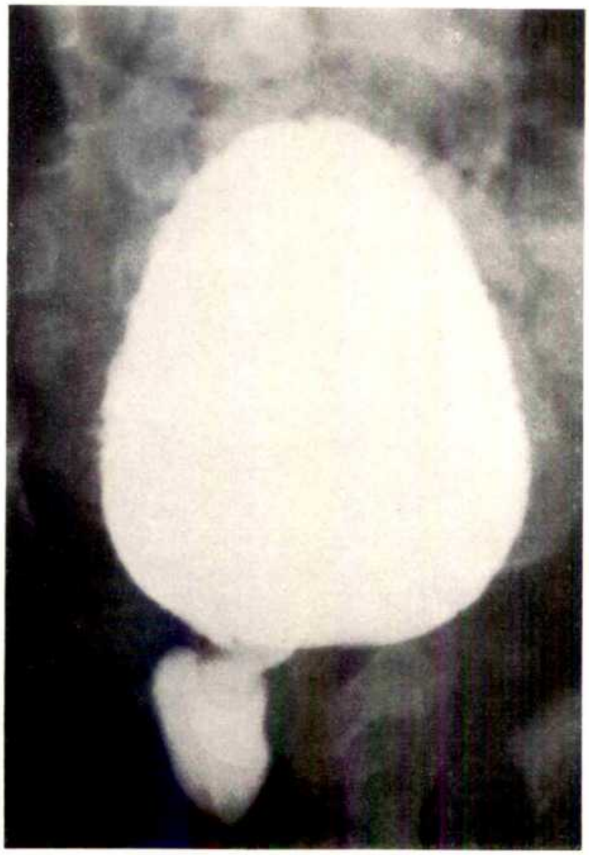


Fig. 8. Micturating cystogram of boy with duplex ureter opening ectopically and with a ureterocele.

pathological conditions, such as dysembryoplasia, which are said to occur at its lower end. Indeed, there are many advantages in preserving it and therefore every reason to do so (Table V). Because the maximum length of ureter is available, there is no tension on the anastomosis and there is never any need to mobilise the ureter far; advancement of the orifice, if this is necessary, is easy to do; the original orifice is, of course, also preserved and, because the cuff of mucosa around it is much wider than the ureter itself, none of the stitches need ever encroach upon the orifice itself. There is, therefore, never any need to splint the ureter.

If the lower end of the ureter is preserved and a combined extravesical and intravesical approach is used, re-implantation of the ureter becomes a satisfying, workmanlike operation which is easy to teach and gives consistently good results.

Summary

For 10 years a modified Politano-Leadbetter technique with extravesical as well as intravesical exposure has been used for re-implantation of the ureter.

The results suggest that the passive mechanism of prevention of reflux is more important than any active mechanism and that it is unnecessary to excise the lower end of the ureter.

We wish to thank Miss Mary Brown for the drawings of re-implantation of the ureter.

References

BELL, C. (1812). Account of the muscles of the ureters. *Medico-Chirurgical Transactions*, **3** (2nd ed., 1816), 171-190.

BROCK, A. J. (1916). *Galen: On the Natural Faculties*. (Loeb's Classical Series.) London: Heinemann, pp. 59 and 60.

PAQUIN, A. J. (1959). Ureterovesical anastomosis: the description and evaluation of a technique. *Journal of Urology*, **82**, 573-583.

POLITANO, V. A. and LEADBETTER, W. F. (1958). An operative technique for the correction of vesicoureteral reflux. *Journal of Urology*, **79**, 932-941.

SAMPSON, J. A. (1903). Ascending renal infection; with special reference to the reflux of urine from the bladder into the ureters as an etiological factor in its causation and maintenance. *Johns Hopkins Hospital Bulletin*, **14**, 334-352.

STEPHENS, F. D. and LENAGHAN, D. (1963). *Congenital Malformations of the Rectum, Anus and Genitourinary Tracts*, edited by F. D. Stephens. Edinburgh: Livingstone, pp. 132-152.

TANAGHO, E. A., GUTHRIE, T. H. and LYON, R. P. (1969). The intravesical ureter in primary reflux. *Journal of Urology*, **101**, 824-832.

TANAGHO, E. A. and HUTCH, J. A. (1965). Primary reflux. *Journal of Urology*, **93**, 158-164.

The Authors

Philip Clark, MD, MChir, FRCS, Consultant Urologist.

R. U. Hosmane, FRCSE (now Resident in Urology, Philadelphia General Hospital, Philadelphia, Pennsylvania, USA).

British Journal of Urology (1976), **48**, 38 ©

Short Case Report

Ureteric Invasion by Endometriosis

Abeshouse and Abeshouse (1960) reviewed the literature on endometriosis of the urinary tract and could find only 15 cases of endometriosis of the ureter. The lesion can be "extrinsic", that is to say, that masses of endometriosis constrict the ureter so that when it is freed from the mass it returns to normal, or it can be "intrinsic" where the ureter is actually invaded by the endometriosis.

Case Report

A 50-year-old pre-menopausal married woman was seen in September 1974 complaining of (*a*) post-coital bleeding for 6 months and (*b*) menorrhagia and metrorrhagia of 2 months' duration.

Vaginal examination revealed a carcinoma of the cervix which it was decided to treat by a combination of radium and surgery.

On 25 September an excretion urogram revealed a normal left urinary tract but the right urinary tract showed dilatation of the pelvicalyceal system and ureter down to the level of the brim of the pelvis. Radium was applied to the cervix.

At laparotomy on 4 December, 1974 for radical hysterectomy and node dissection, an area of endometriosis, the size of a pinhead, was found on the anterior surface of the left broad ligament adjacent to the round ligament. On the right side of the pelvis, on the posterior peritoneum, over the right utero-sacral ligament, near to its junction with the rectum and at the brim of the pelvis, there were 3 very small areas of endometriosis and, underlying this in the connective tissue, was an area of endometriosis, approximately 1·2 cm in diameter. On dissection, this was found to extend to the right ureter and to invade its outer coats obviously causing the stricture shown on the urogram. Even when the ureter had been completely freed, the stricture remained, due to the fact that the endometriosis was perforating the wall of the ureter. The ureter below the stricture was normal in size. There was no evidence of malignant involvement of the ureter. The histological appearances of the endometriosis removed from the ureter are shown in the Figure.

As both ovaries were to be removed as part of the radical hysterectomy, it was decided to wait and see if the endometriosis subsided after operation.

15 weeks later an excretion urogram showed a normal urinary tract on both sides.

Comment

This case is an example of "intrinsic" endometriosis of the ureter.

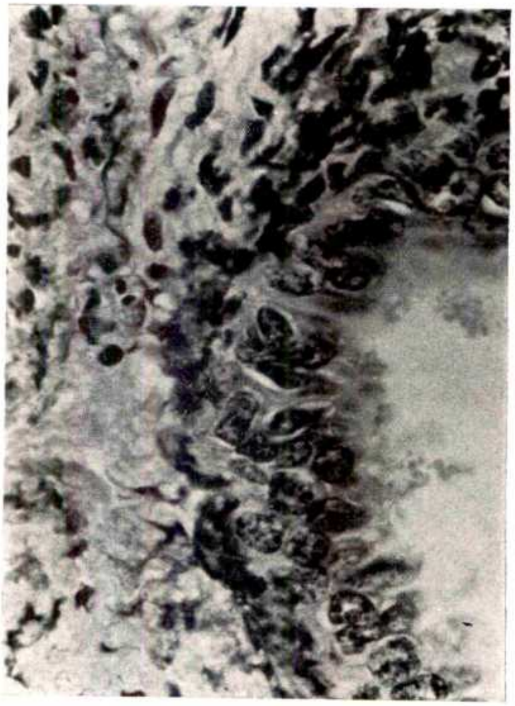
It is of interest that Dick *et al.* (1973) recorded a case of endometriosis involving the ureter in a post-menopausal woman in which the disease was reactivated by the administration of a synthetic oestrogen resulting in ureteric obstruction.

Stanley Way and J. R. Young,
Departments of Gynaecological Oncology, and Diagnostic Radiology, Queen Elizabeth Hospital, Gateshead

References

Abeshouse, B. S. and Abeshouse, G. (1960). Endometriosis of the urinary tract: a review of the literature. *Journal of the International College of Surgeons*, **83**, 100-102.

Dick, A. L., Lang, D. W., Bergman, R. T., Bhatnaghar, B. N. S. and Selvaggi, J. F. P. (1973). Post-menopausal endometriosis with ureteric obstruction. *British Journal of Urology*, **45**, 153-155.



British Journal of Urology (1976), **48**, 39-42 ©

First Report on the Standardisation of Terminology of Lower Urinary Tract Function

PRODUCED BY THE INTERNATIONAL CONTINENCE SOCIETY, FEBRUARY, 1975[1]

Members: Patrick Bates, William E. Bradley, Eric Glen, Hansjörg Melchior, David Rowan, Arthur Sterling and Tage Hald (Chairman)

This report contains the first set of recommendations dealing with the terminology of lower urinary tract function. Specifically, it covers the storage of urine in the bladder, urinary incontinence and units of measurement. The recommendations were subject to discussion during the Fourth Annual Meeting of the International Continence Society in Mainz, Germany in September, 1974.

These standards are proposed to facilitate comparison of results by investigators who use urodynamic methods. It is recommended that the acknowledgement of these standards in written publications be indicated by a footnote to the section "Methods and Material" or its equivalent:

"Methods, definitions, and units conform to the standards proposed by the International Continence Society except where specifically noted."

Urinary Incontinence

Incontinence is a condition where involuntary loss of urine is a social or hygienic problem and is objectively demonstrable. Loss of urine through channels other than the urethra is extra-urethral incontinence.

Stress Incontinence denotes:
1. a symptom,
2. a sign, and
3. a condition = genuine stress incontinence.

The *Symptom* "stress incontinence" indicates the patient's statement of involuntary loss of urine when exercising physically (in the broadest possible sense of the words).

The *Sign* "stress incontinence" denotes the observation of involuntary loss of urine from the urethra immediately upon an increase in abdominal pressure.

The *Condition* "genuine stress incontinence" is involuntary loss of urine when the intravesical pressure exceeds the maximum urethral pressure but in the absence of detrusor activity.

Urge Incontinence is involuntary loss of urine associated with a strong desire to void. Urge incontinence may be subdivided into *Motor Urge Incontinence*, which is associated with uninhibited detrusor contractions, and *Sensory Urge Incontinence* which is not due to uninhibited detrusor contractions.

Reflex Incontinence is voluntary loss of urine due to abnormal reflex activity in the spinal cord in the absence of the sensation usually associated with the desire to micturate.

Overflow Incontinence is involuntary loss of urine when the intravesical pressure exceeds the maximum urethral pressure due to an elevation of intravesical pressure associated with bladder distension but in the absence of detrusor activity.

Procedures Related to the Evaluation of Urine Storage

Cystometry

Cystometry is the method by which the pressure-volume relationship of the bladder is measured. Zero reference for pressure is the level of the superior edge of the symphysis pubis.

---

[1] Revised following discussion during the business meeting of the International Continence Society, Mainz, 1974.

Specify: Access: 1. transurethrally,
2. percutaneously.
Medium: 1. liquid,
2. gas.
Temperature: state temperature in degrees Celsius.
Position of patient: 1. supine,
2. sitting,
3. standing.
Filling: 1. continuous,
2. incremental.
The precise filling rate should be stated.[2] When using incremental method, also state volume of increment.

Technique:

1. single or double lumen catheter or multiple catheters,
2. type of catheter (manufacturer),
3. size of catheter,
4. measuring equipment.

Findings: Before starting to fill, residual urine should be measured. The presence of contractions exceeding 15 cm H_2O clearly indicates an uninhibited detrusor contraction when the patient has been asked to inhibit. Pressure elevations smaller than 15 cm H_2O indicate that clinical judgement should be exercised. An indication of the volume at first desire to void should be made.

Maximum Cystometric Capacity is the volume at which the patient has a strong desire to void.

Effective Cystometric Capacity is the maximum cystometric capacity minus the residual urine.

Compliance indicates the change in volume for a change in pressure. It is defined as $C = \Delta V \Delta p$ where ΔV is the volume increment and Δp is the change in pressure associated with this volume increment. During cystometry, it is taken for granted that the patient is awake and not sedated. If otherwise, this should be specified.

Urethral Closure Pressure Profile

Urethral closure pressure profile denotes the intraluminal pressure along the length of the urethra with the bladder at rest.

Zero reference for pressure is the level of the superior edge of the symphysis pubis.

To be meaningful, bladder pressure should be measured simultaneously.

Specify:

1. catheter type and size,
2. measurement technique,
3. rate of infusion,
4. continuous or intermittent withdrawal,
5. rate of withdrawal,
6. bladder volume,
7. position of patient: (*a*) supine,
    (*b*) sitting,
    (*c*) standing.

Findings (see Fig.):

Maximum urethral pressure is the maximum pressure of the measured profile.

Maximum urethral closure pressure is the difference between the maximum urethral pressure and the bladder pressure.

Functional profile length is the length of the urethra along which the urethral pressure exceeds bladder pressure. (*Total profile length* is not generally regarded as a clinically useful parameter.)

Units of Measurement

In current urodynamic literature there is no standardisation in the units of measurement. For example, intravesical pressure is sometimes measured in mm Hg and sometimes in cm H_2O. When Laplace's law is used to calculate tension in the bladder wall, it is often found that pressure is then measured in dyne cm^{-2}. This lack of uni-

---

[2] For general discussion, the following terms for the range of filling rate may be used:
1. up to 10 ml per minute is a *slow fill cystometry*;
2. 10-100 ml per minute is a *medium fill cystometry*;
3. over 100 ml per minute is a *rapid fill cystometry*.

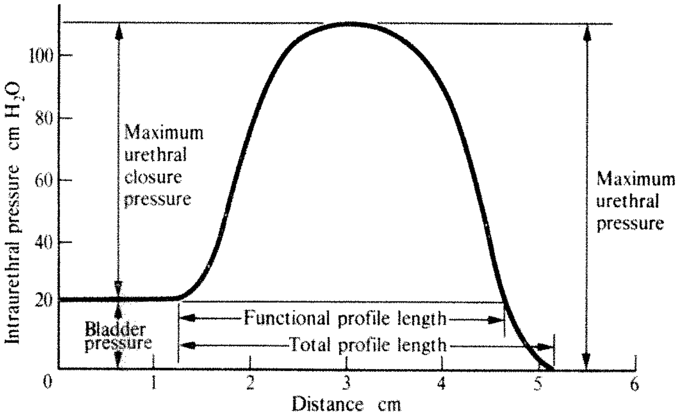


Fig. A schematic representation of the urethral closure pressure profile.

formity in the systems used leads to confusion when other parameters, which are a function of pressure, are computed, for instance, "compliance", "urethral resistance", etc. From these few examples it is evident that standardisation is essential for meaningful communication. Many journals now require that the results be given in SI Units.

This system will be used in all future I.C.S. papers. The following report is designed to give guidance in the application of the SI system to urodynamics and defines the units involved. The principal units to be used are listed below. A fuller explanation of the SI system is given in Appendix A.

Quantity	*Acceptable Unit*	*Symbol*
volume	millilitre	ml
time	second	s
flowrate	millilitres/second	ml s^{-1}
pressure	centimetres of water[3]	cm H_2O
length	metres or submultiples	m, cm, mm
velocity	metres/second or submultiples	m s^{-1}, cm s^{-1}
temperature	degrees Celsius[4]	°C

Appendix A

Le Système International d'Unités (SI Units)

At the Conférence Générale des Poids et Mesures (CGPM) in Paris in 1960 it was agreed internationally that this system of units (abbreviated to SI in all languages) should be adopted for all scientific and technical work. It is an extension and refinement of the traditional metric system and is rational, coherent and comprehensive. It is therefore logical that this system should be used in all urodynamic studies.

There are 7 fundamental units; all other units are derived from these. The 3 basic mechanical quantities are mass, length and time. The complete list is given below.

Quantity	*Unit*	*Symbol*
mass	kilogramme	kg
length	metre	m
time	second	s
temperature	kelvin	K
electric current	ampere	A
luminous intensity	candela	cd
amount of substance	mole	mol

---

[3] The SI Unit is the pascal, but it is only practical at present to calibrate our instruments in cm H_2O. One centimetre of water pressure is approximately equal to 100 pascals (1 cm H_2O = 98·07 Pa). When calculating parameters that are a function of pressure, for example, "compliance", the pascal must be used to avoid confusion. Measurements reported in millimetres of mercury will not be acceptable.

[4] The SI Unit is the degree Kelvin. The Kelvin temperature interval is identical with the degree Celsius (centigrade) temperature interval. The Kelvin scale starts at absolute zero (−273·16°C), and this is inconvenient in medical practice. The Celsius scale will therefore be used.

As in the metric system a prefix may be added to the unit to indicate that a multiplier of the form 10^a has been applied.

Prefix	*Symbol*	*Multiplier*	*Remarks*
tera	T	10^{12}	
giga	G	10^9	
mega	M	10^6	
kilo	k	10^3	
hecto	h	10^2	1
deca	da	10^1	1
deci	d	10^{-1}	1, 2
centi	c	10^{-2}	1, 3
milli	m	10^{-3}	
micro	μ	10^{-6}	
nano	n	10^{-9}	
pico	p	10^{-12}	

Remarks

1. An endeavour is being made to reduce unnecessarily fine division by discouraging the general use of exponent values, $a = +2, +1, -1, -2$.
2. The prefix "deci" may be used to specify a volume of $10^{-3}m^3 = 1\ dm^3$ since the litre has been redefined as $1\ dm^3$ exactly.
3. Although "centi" is one of the discouraged prefixes, it is too well established to be eliminated at the present time.

Derived SI Units

These units are composed of combinations of the fundamental units; some of them have been given special names.* A few examples of commonly used units are listed below.

area	= $(\text{length})^2$	= m^2	= *square metre*
volume	= $(\text{length})^3$	= m^3	= *cubic metre*[1]
flowrate	= volume per unit time	= m^3s^{-1}	= *cubic metres per second*[2]
density	= mass per unit volume	= $kg\ m^{-3}$	= *kilogrammes per cubic metre*
velocity	= distance in unit time	= $m\ s^{-1}$	= *metres per second*
acceleration	= velocity increase in unit time	= $m\ s^{-2}$	= *metres per second per second*
force	= mass × acceleration	= $kg\ m\ s^{-2}$	= *newton* (N)*
energy	= force × displacement	= N m	= *joule* (J)*
power	= energy per unit time	= $N\ m\ s^{-1}$	= *watt* (W)*
pressure	= force per unit area	= $N\ m^{-2}$	= *pascal* (Pa)*
stress	= force per unit area	= $N\ m^{-2}$	= *pascal* (Pa)*
tension	= force per unit length	= $N\ m^{-1}$	= *newtons per metre*
momentum	= mass × velocity	= $kg\ m\ s^{-1}$	= *kilogramme metres per second*
electric charge	= electric current × time	= A s	= *coulomb* (C)*
potential difference	= energy to move 1 coulomb	= joules per coulomb	= *volt* (V)*
electric resistance	= potential difference for 1 ampere	volt per ampere	= *ohm* (Ω)*

Use of SI Units and their Multiples

The symbol of a prefix is considered to be combined with the unity symbol to which it is directly attached forming a new unit symbol which can be raised to a positive or negative power.

$$e.g.,\ 1\ cm^3 = (10^{-2}m)^3 = 10^{-6}m^3$$
$$1\ kN\ m^{-2} = 10^3N\ m^{-2}$$

When expressing a quantity by a numerical value and a certain unit, it has been found convenient to use units resulting in numerical values between 0·1 and 1000.

$$e.g.,\ 14300\ N = 14{\cdot}3\ kN$$
$$0{\cdot}00564\ m = 5{\cdot}64\ mm$$

---

[1] Another unit which is accepted is *litre* = $1\ dm^3$.

[2] Another unit which is accepted is *litres per second* = $dm^3\ s^{-1}$.

British Journal of Urology (1976), 48, 43-53 ©

Innervation of the Muscle of the Bladder in the Rat

A. D. HOYES, R. BOURNE and B. G. H. MARTIN
Department of Anatomy, St Mary's Hospital Medical School, London

Although it has recently been shown (Elbadawi and Schenk, 1966; Schulman, Duarte-Escalante and Boyarsky, 1972; Raezer *et al.*, 1973; Dixon and Gosling, 1974) that there are large numbers of adrenergic axons in the vesical nerves, these have been found to be mainly distributed to the muscle at the base of the bladder and it is still widely accepted that the remainder of the detrusor receives the majority of its efferent innervation from cholinergic axons. The ultrastructure of the axonal terminals (Caesar, Edwards and Ruska, 1957; Thaemert, 1963; Fletcher, Hammer and Bradley, 1969; Dixon and Gosling, 1974) and the high output of acetylcholine that occurs during stimulation of the vesical nerves (Carpenter and Rand, 1965; Chesher, 1967) are consistent with the innervation of the detrusor mainly by cholinergic axons, but there are a number of aspects of the pharmacology of neuromuscular transmission in the bladder which differ from those normally associated with cholinergic innervation, and these are such that a number of authors (Henderson and Roepke, 1934; Chesher and Thorp, 1965; Ambache and Zar, 1970; Dumsday, 1971) have concluded that impulse transmission is mediated, at least in part, by substances other than acetylcholine. While it is possible that the discrepancy between the evidence that has been obtained from pharmacological investigation and that derived from other methods of approach is partly due to factors such as the interaction between functionally distinct axons discussed by Dixon and Gosling (1974), other recent studies have provided 2 alternative explanations for these findings. The demonstration of scattered small dense-cored vesicles in the otherwise cholinergic terminals of axons innervating the muscle (Hoyes, Bourne and Martin, 1974) has raised the possibility of the existence at these terminals of a pattern of dual transmitter action not unlike that proposed by Koelle (1961) for the adrenergic axon, and the effect of drugs such as quinidine on neuromuscular transmission (Burnstock, Dumsday and Smythe, 1972) has been related to the innervation of the muscle by a separate population of axons which, because they are thought to employ ATP as a transmitter, have been called purinergic (Burnstock, 1972). The extent to which these 2 types of axon contribute to the innervation of the muscle is, however, still in doubt. Previous studies have provided widely different figures for the density of innervation of the muscle (see Elbadawi and Schenk, 1966) and, although axons with terminals of the kind classified as purinergic have been demonstrated in relation to smooth muscle cells in a number of tissues, their presence and distribution in the intramuscular plexuses of the bladder have not yet been clearly established. The terminals of both these and the various other types of axon which have been implicated in the innervation of smooth muscle can all be clearly distinguished at the ultrastructural level and we have recently employed quantitative ultrastructural techniques to study the patterns of innervation of the ureter in the rat (Hoyes, Bourne and Martin, 1975*a*, *b*). We are now applying similar methods of approach to the analysis of the innervation of the bladder of the rat, and in the present investigation we have examined the structure and composition of the nerves associated with the muscle of the body of the bladder in this species.

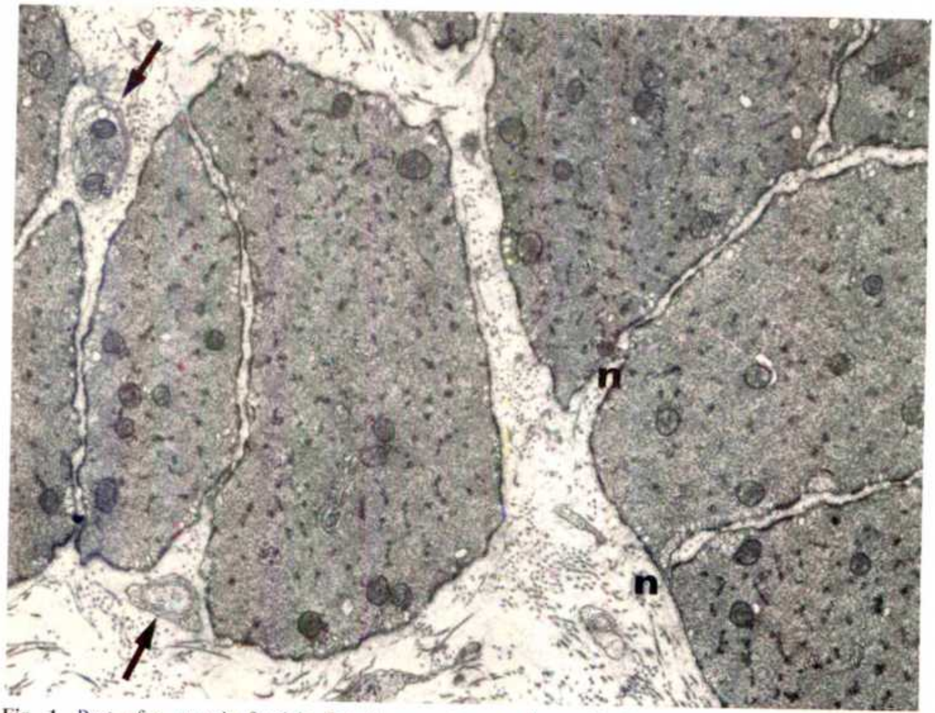


Fig. 1. Part of a muscle fascicle. Small nerves (arrowed) are distributed between the muscle cells. n, nexal contacts between adjacent cells. × 8,500.

Materials and Methods

Specimens of bladder were obtained from 12 young adult male Wistar rats. The animals were anaesthetised with Nembutal and, in order to facilitate the identification of adrenergic axonal terminals, were given intravenous injections of 100 mg/kg 6-hydroxydopamine ½ to 2 hours before death. Fixation was begun by perfusion of the animals through the descending aorta with Karnovsky's (1965) fixative. Blocks were then removed from the anterolateral surface of the bladder body approximately midway between base and apex and immersed in fresh fixative for 1 hour. They were then post-fixed in unbuffered osmium tetroxide, stained in bulk with uranyl acetate, dehydrated in ethyl alcohol and embedded in TAAB resin. Ultrathin sections cut on a Huxley ultramicrotome were mounted on uncoated grids, stained with lead citrate and examined in a Siemens Elmiskop I electron microscope.

The structure and composition of the infrafascicular nerves was studied in random micrographs taken at an initial magnification of × 2,000 and printed at a final magnification of × 5,000. The density of innervation of the muscle was also computed from these micrographs, counts of the number of muscle cells and nerves being obtained from the prints by applying to them a standard procedure similar to that employed for counting blood cells in a haemocytometer. The size and terminal density of the interfascicular nerves was estimated without photographic reproduction, counts being made at the microscope of all the nerves encountered in sections from 3 blocks for each animal.

Results

The architecture of the detrusor in the animals studied corresponded closely to that observed

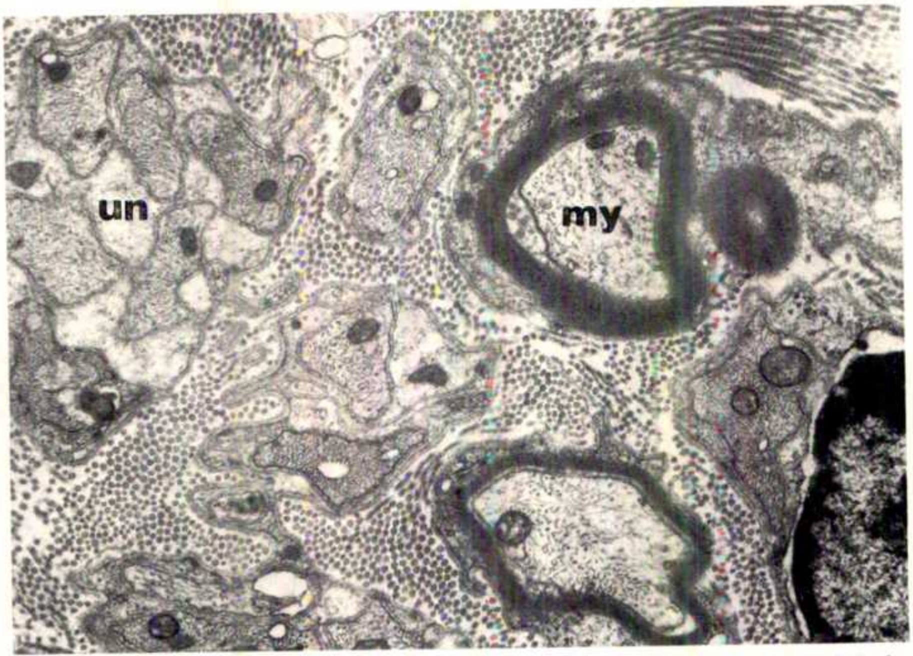


Fig. 2. Part of a large interfascicular nerve. In addition to numerous unmyelinated axons (un), the nerve contains several myelinated axons (my). × 17,000.

in other species and in man. The muscle cells were organised into interlacing fascicles which often showed evidence of branching. Adjacent fascicles were often aligned more or less in the same direction, but there was only limited evidence of their arrangement into definite layers. The cells forming the fascicles were morphologically indistinguishable from typical smooth muscle cells and small areas of close approximation of the membranes with the features of punctate nexuses were fairly common (Fig. 1).

Of the nerves encountered between the muscle fascicles, the largest were surrounded by a perineurial sheath and sometimes contained one or more myelinated axons (Fig. 2). Smaller nerves were invariably formed only by unmyelinated axons and were devoid of a perineurial sheath. Branches of these nerves were often located close to arterioles, and the arterioles were also provided with a fine periarteriolar plexus which, as in the corresponding vessels in the ureter (Hoyes, Bourne and Martin, 1975*b*), was located between the connective tissue cell sheath surrounding the vessels and the medial muscle cells. Other branches of the interfascicular nerves were situated close to the surface of the fascicles of detrusor muscle cells. Of these, a small proportion appeared to be in the process of entering the fascicles and of breaking up into branches containing between 1 and 3 axons (Fig. 3). The occasional nerves of this kind seen in the sections were included in the counts of the interfascicular nerves, but in each case the group of small branches was regarded as a single nerve. In spite of this and the fact that the nerves in the periarteriolar plexuses were excluded from the counts, it was found that a high proportion of the interfascicular nerves contained between 2 and 4 axons (Fig. 4) and that, although some nerves without a perineurial sheath contained more than 30 axons, the mean size of all such nerves was only 6·4 (Table).

The intrafascicular nerves were generally aligned parallel to the muscle cells and were more or less evenly distributed in the fascicles. The majority contained only 1 axon (Fig. 4) and the mean number of axons in the nerves encountered in the micrographs from the 12 animals studied was 1·3 (Table). The figures obtained from these micrographs for the density of innervation of the muscle were much lower than those obtained for arteriolar muscle in the ureter (Hoyes,

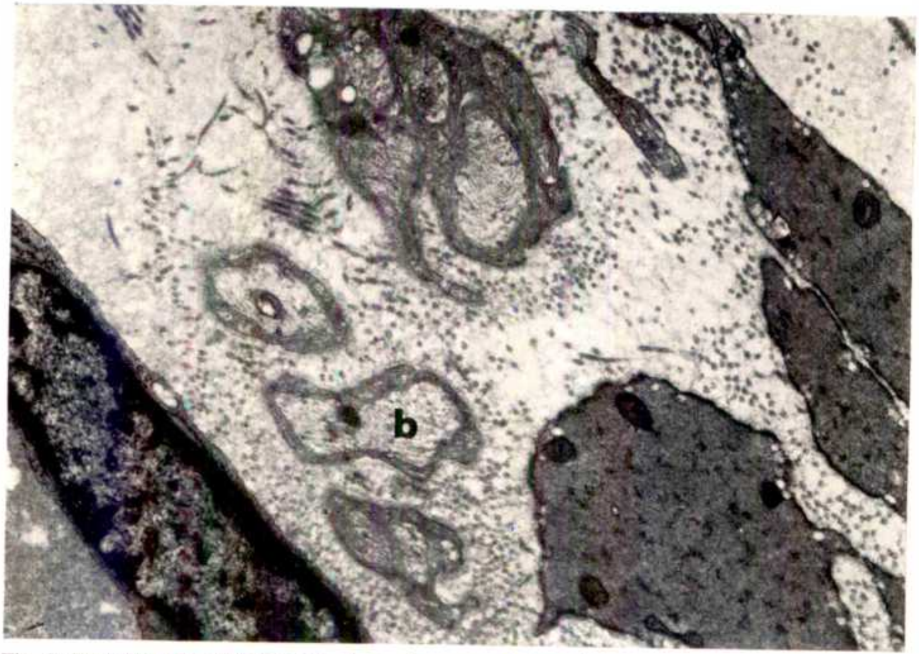


Fig. 3. Small branches (b) of an interfascicular nerve at the point of entry into a muscle fascicle. × 17,000.

Bourne and Martin, 1975*b*), there being only 14·7 ± 3·2 nerves and 19·2 ± 4·8 axons/100 muscle cells.

4 types of terminal varicosity were seen in the nerves ramifying within and between the fascicles of muscle cells. Only 2 terminals in which accumulations of mitochondria almost completely filled the axoplasm were seen and both of these were present in interfascicular nerves. Terminals which contained the numerous small dense-cored vesicles characteristic of adrenergic axonal varicosities were common in the perivascular networks. They were also occasionally present in

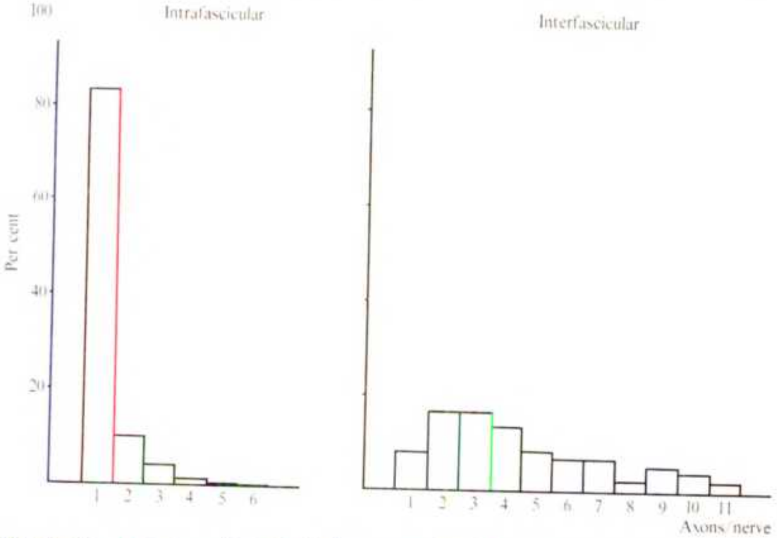


Fig. 4. Size of intra- and interfascicular nerves. 8·4% of the interfascicular nerves contained more than 11 axons.

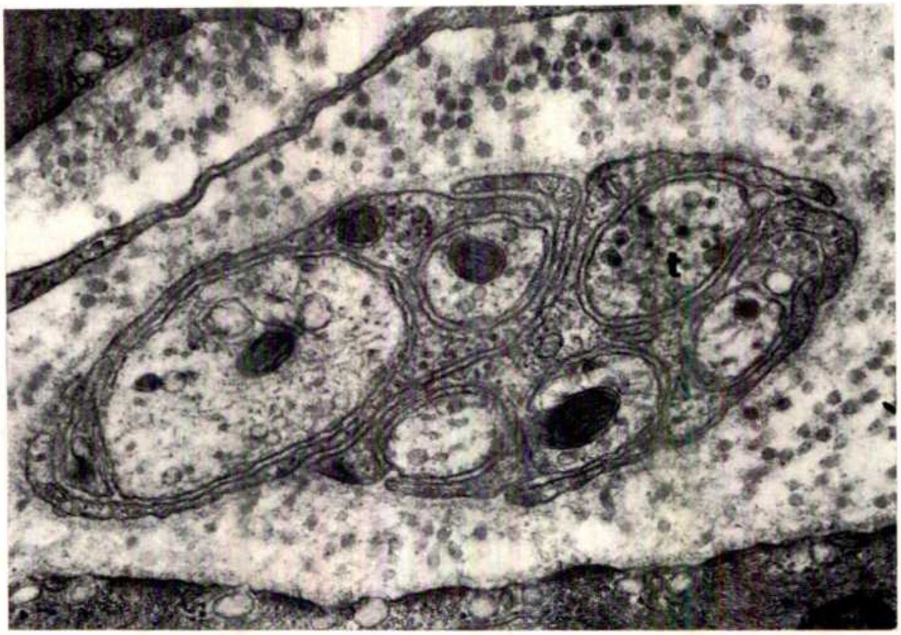


Fig. 5. Adrenergic axonal terminal (t) in an intrafascicular nerve. From an animal given 6-OHDA 1 hr previously. × 41,000.

the intrafascicular nerves (Fig. 5) but were never seen in nerves situated in an interfascicular position.

The third type of terminal was represented by a fusiform enlargement which contained numerous closely packed clear vesicles of approximately the same size as those present in the cholinergic terminal (Fig. 6). In addition to mitochondria and scattered large dense-cored vesicles, the terminals contained occasional small dense-cored vesicles (Fig. 7). In animals perfused ½ to 1 hour after administration of 6-hydroxydopamine, such vesicles were present in up to half of the terminal profiles. Their core was sometimes very small but in many it almost completely filled the vesicle lumen (Fig. 7). In the intrafascicular nerves, the membrane in the terminal region was often only partially covered by the Schwann cells. At such sites, the axonal membrane was often closely related to that of adjacent muscle cells (Figs. 6 and 7) but the approximation of the two membranes was rarely sufficiently close to exclude the basement membrane. The density of this third type of terminal was high in the intrafascicular nerves and was significantly different to that in the interfascicular nerves, in which the terminals were only present in very small numbers (Table).

Table

Size and Terminal Density of the Inter- and Intrafascicular Nerves in the Body of the Bladder of 12 Rats

		Terminals/100 axons		
	Axons/nerve	Cholinergic	Adrenergic	Sensory
Interfascicular nerves	6·4 ± 2·6†	3·8 ± 2·7	0·0	17·2 ± 6·9
Intrafascicular nerves	1·3 ± 0·2*	35·1 ± 4·2*	0·4 ± 0·3	2·9 ± 2·4*

† Mean and standard deviation.
Starred figures are significantly different from those for the interfascicular nerves ($P < 0{\cdot}001$).

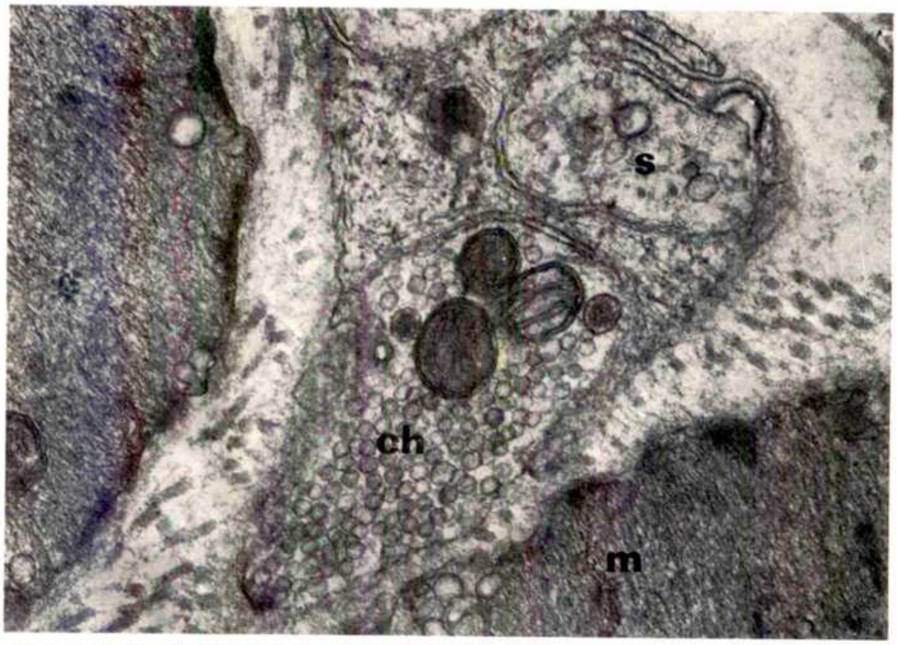


Fig. 6. Part of an intrafascicular nerve showing 2 distinct types of axonal terminal. The cholinergic terminal (ch) contains only small clear and large dense-cored vesicles, and part of the axonal membrane is closely related to that of an adjacent muscle cell (m). The second terminal (s) is completely surrounded by leaflets of the Schwann cell cytoplasm and contains only scattered clear vesicles of variable size. From an animal given 6-OHDA 2 hr previously. ×41,000.

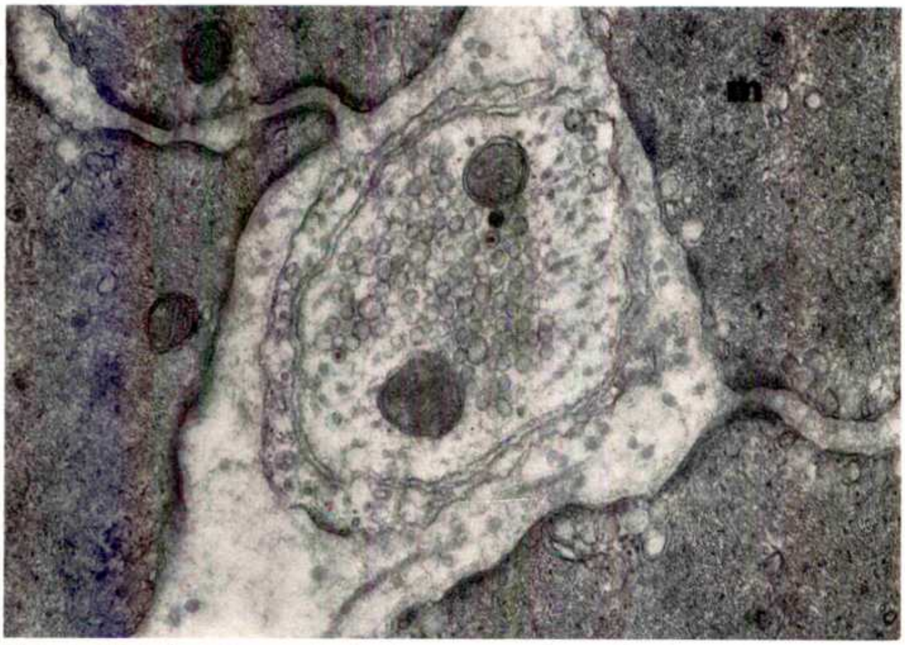


Fig. 7. Small intrafascicular nerve. In addition to numerous clear vesicles, the terminal contains some small dense-cored vesicles, and, as in Figure 6, the exposed part of the axonal membrane is closely related to that of an adjacent muscle cell (m). From an animal given 6-OHDA 1 hr previously. ×42,500.

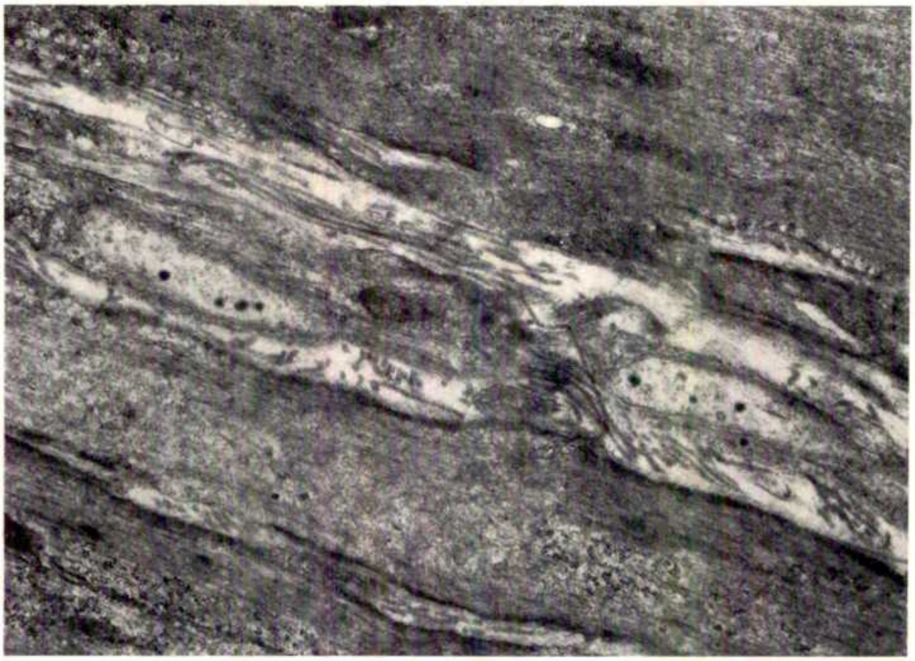


Fig. 8. Oblique section through 1 of the larger intrafascicular nerves showing 2 terminals containing large dense-cored vesicles. From an animal given 6-OHDA 1 hr previously. × 20,000.

The 4th type of terminal was identical to that demonstrated in the submucous plexuses of the ureter (Hoyes, Bourne and Martin, 1975*a*). As in the ureteric nerves, the terminals contained variable numbers of both clear and large dense-cored vesicles. The dense-cored vesicles were sometimes fairly numerous and, in these cases, the terminals were indistinguishable from those classified by Burnstock (1972) as purinergic. The majority of the terminals contained relatively few vesicles of this kind (Fig. 8) and in some profiles the vesicles were absent (Fig. 6). Terminal profiles devoid of dense-cored vesicles usually contained some clear vesicles but, because these were generally few and varied considerably in size, the terminals could almost invariably be distinguished without difficulty from the other types of terminal in the nerves (Fig. 6). Most of the terminals encountered in the intrafascicular nerves were completely covered by leaflets of Schwann cell cytoplasm (Fig. 6) and even in cases in which part of the membrane was left uncovered, the interval between the membrane and that of adjacent muscle cells was rarely less than 100 nm. The terminals were also usually located in the larger of the intrafascicular nerves (Figs. 6 and 8) and their mean density in the intrafascicular networks was significantly lower than in the nerves situated between the muscle bundles (Table).

Discussion

The structure and organisation of the nerves associated with the vesical detrusor demonstrated in the present investigation can be related to the innervation of the muscle by two separate subplexuses. Of these, one is represented by the intrafascicular nerves and the second is formed by nerves which ramify in the interfascicular connective tissue. The intrafascicular networks are formed by branches of larger nerves which, at about the point where they enter the fascicles, divide into small branches containing between 1 and 3 axons. It is probable that, apart from those already showing evidence of branching, a significant proportion of the nerves seen in the interfascicular connective tissue were ultimately destined to ramify within the muscle fascicles but the small size of many of the nerves and their radically different patterns of terminal organisation suggests that the majority form the components of a separate and functionally distinct network.

The structure of the intrafascicular networks is consistent with that of the predominantly efferent plexuses in the smooth muscle of other tissues. The plexuses associated with the muscle of the vas deferens (Yamauchi and Burnstock, 1969) and ureteric arterioles (Hoyes, Bourne and Martin, 1975*b*) are also characterised by small nerves with a high terminal density, and the only major difference between these plexuses and the nerves supplying the detrusor is that they appear to provide the muscle with a much higher level of innervation. Previous estimates of the density of innervation of the vesical detrusor have ranged between 1 and 200-400 nerve fibres/100 muscle cells (Elbadawi and Schenk, 1966). The figures obtained in the present investigation are indicative of a level of detrusor innervation which is intermediate between these 2 extremes and are consistent with the classification of the muscle in the middle of the 3 types proposed by Burnstock (1970). The fairly frequent occurrence of the nexuses which probably represent the sites of functional continuity through which electrotonic coupling is established between muscle cells affords further support for such a classification, and also provides a basis for the co-ordinated contraction of the detrusor that occurs during voiding.

The infrequent occurrence of adrenergic axonal terminals in the intrafascicular networks is in accord with the observations made by Elbadawi and Schenk (1966) in their careful and comprehensive light microscopical study of the innervation of the bladder. The presence of numerous terminals of this kind on axons of the perivascular nerves is also in agreement with the findings of these authors and, although insufficient vessels were observed to permit a quantitative analysis of their innervation, there appeared to be a fairly close resemblance between their nerve supply and that of the small vessels of the ureter (Hoyes, Bourne and Martin, 1975*b*).

The close correspondence between the density of the terminals containing closely packed clear vesicles in the intrafascicular nerves and that found for adrenergic terminals in the periarteriolar plexuses of the ureter (Hoyes, Bourne and Martin, 1975*b*) implies that axons with such terminals constitute a very high proportion of those ramifying in the nerves and the frequent occurrence of the close approximation between the exposed parts of the membrane of the terminals and that of adjacent muscle cells which is usually regarded as necessary for effective neuromuscular transmission indicates that they play an important, if not major, role in the efferent control of detrusor activity. The clear vesicles in the terminals were indistinguishable from those present in the terminals of efferent cholinergic axons, and the only difference between the terminal profiles and sections through those of cholinergic axons was the presence in a proportion of scattered small dense-cored vesicles. The silver to pale gold sections normally employed for transmission electron microscopy probably have a thickness of less than 90 nm and the identification of such vesicles in only up to 50% of the profiles may be related more to their presence in only small numbers and wide dispersal in the terminals than to the existence within the nerves of 2 functionally distinct types of axon. The vesicles were in general about the same size as those in the terminals of adrenergic axons but their core often occupied much more of the lumen. The core also appears to be less susceptible to extraction by glutaraldehyde than that of the vesicles in the adrenergic terminal but their pattern of response to 6-hydroxydopamine (Hoyes, Bourne and Martin 1974), suggests that they contain a similar form of monoamine.

Although the extent to which the material contained in the small dense-cored vesicles in the otherwise apparently cholinergic terminals contributes to transmission of the nerve impulse is still conjectural, its involvement with acetylcholine in this process may account for many, if not all, of the atypical features of neuromuscular transmission in the bladder. Of these, the most well-known is the resistance of nerve-mediated responses to atropine. It has recently been shown that atropine releases acetylcholine from the cerebral cortex (Cooper, Bloom and Roth, 1974) and its limited action at the motor end plates of striated muscle has been attributed to non-specific effects (Katz and Miledi, 1973). There is, however, no reason to suppose that atropine has similar actions at the neuromuscular junctions in smooth muscle and it is almost universally accepted that the block of impulse transmission produced by this drug in most cholinergically innervated smooth muscles is due to competitive inhibition of acetylcholine at the site of the receptors on the muscle cells. In this event, it is unlikely that any second transmitter present in the small dense-cored vesicles operates in exactly the same manner as that postulated by Koelle (1961) for acetylcholine at the adrenergic terminal. If, however, rather than acting back on the axonal membrane, the transmitter couples to the membrane of the muscle cells it is possible that this evokes the formation of receptors for acetylcholine which are resistant to the action of atropine. Such considerations do not preclude the presence of the normal type of muscarinic receptor on the cells and the effectiveness of atropine in blocking the action of exogenously applied acetylcholine (see, for example, Henderson and Roepke, 1934; Chesher and Thorp, 1965; Huković, Rand and Vanov, 1965; Ambache and Zar, 1970) implies that there are at least moderate numbers of such receptors in the muscle.

Although, at one extreme of their range of vesicle content, the terminals of the 4th type identified in the nerves were morphologically indistinguishable from those classified by Burnstock (1972) as purinergic, their distribution in the nerves differed markedly from that expected of the terminals of efferent axons. There was also very little indication of a close association of the terminals with the membranes of the muscle cells, and the majority were completely surrounded by the Schwann cells. Those present in the intrafascicular networks were concentrated in the larger nerves and the much higher density of the terminals in the interfascicular nerves suggests that most of the axons with which they are associated terminate within these networks. Degenerating terminals with a similar vesicle content have also been identified in the vesical nerves following dorsal root section in the cat (Uemura, *et al.*, 1973; Uemura, Fletcher and Bradley, 1974) and the close correlation between the density of the terminals in the 2 major components of the muscular plexus observed in the present study and that of the degenerating terminals found by these authors following section of the sacral dorsal roots provides further support for the concept that they represent the endings of afferent axons. The similar terminals that have been seen in all of the intramural plexuses of the ureter (Hoyes, Bourne and Martin, 1975*a*, *b*) have also been regarded as afferent endings and their high density in the submucous nerves of the ureter (Hoyes, Bourne and Martin, 1975*a*) and frequent occurrence in a number of other nerves, including these of the cornea (Hoyes and Barber, 1975) have been equated with their involvement in pain perception. Axons with the same kind of terminal have as yet not been demonstrated in the human bladder, but we have been able to show that they are widely distributed in the vesical nerves of a number of other species of mammal (Hoyes, Barber and Martin, 1975) and the occurrence of a similar pattern of afferent innervation of the human detrusor to that demonstrated in the present study could well account for the pain response observed by McLellan and Goodell (1943) following the application of electrical and other stimuli to the vesical mucosa.

Summary

A quantitative ultrastructural analysis of the organisation and terminal density of the nerves associated with the muscle of the body of the bladder was undertaken in the rat. The results obtained were suggestive of the organisation of the intramuscular plexuses into 2 separate and possibly functionally distinct networks. The nerves ramifying within the muscle fascicles mostly contained between 1 and 3 axons and on the basis of counts made in 12 animals, appeared to provide the muscle with only a moderate level of innervation. Although adrenergic terminals were frequently seen in the perivascular plexuses, they were rarely encountered in the nerves within the muscle fascicles. The majority of the terminals in the intrafascicular nerves were similar to those normally classified as cholinergic and, in many, the exposed parts of the axonal

membrane were closely related to that of adjacent muscle cells. In addition to clear vesicles and large dense-cored vesicles, many of these terminals contained scattered small dense-cored vesicles. It was suggested that the involvement of the material present in the small dense-cored vesicles with acetylcholine in impulse transmission might account for the atypical features of such transmission in the bladder and in particular its resistance to blockade by atropine. The nerves forming the interfascicular networks contained few axons with cholinergic terminals, and were characterised by much larger numbers of a morphologically distinctive type of terminal. Some of these were indistinguishable from those recently defined as the terminals of purinergic axons but their distribution in the nerves suggests that they represent the terminals of afferent axons and is consistent with the concept that, together with those observed in other tissues, such axons are involved in pain perception.

References

AMBACHE, N. and ZAR, M. A. (1970). Non-cholinergic transmission by post-ganglionic motor neurones in the mammalian bladder. *Journal of Physiology*, **210**, 761-783.

BURNSTOCK, G. (1970). Structure of smooth muscle and its innervation. In *Smooth Muscle*, ed. E. Bülbring, A. F. Brading, A. W. Jones and T. Tomita. London: Edward Arnold, pp. 1-69.

—— (1972). Purinergic nerves. *Pharmacological Reviews*, **24**, 509-581.

BURNSTOCK, G., DUMSDAY, B. and SMYTHE, A. (1972). Atropine resistant excitation of the urinary bladder: the possibility of transmission via nerves releasing a purine nucleotide. *British Journal of Pharmacology*, **44**, 451-461.

CAESAR, R., EDWARDS, G. A. and RUSKA, H. (1957). Architecture and nerve supply of mammalian smooth muscle tissue. *Journal of Biophysical and Biochemical Cytology*, **3**, 867-877.

CARPENTER, F. G. and RAND, S. A. (1965). Relation of acetylcholine release to responses of the rat urinary bladder. *Journal of Physiology*, **180**, 371-382.

CHESHER, G. B. (1967). Acetylcholine in extracts and perfusates of urinary bladder. *Journal of Pharmacy and Pharmacology*, **19**, 445-455.

CHESHER, G. B. and THORP, R. H. (1965). The atropine-resistance of the response to intrinsic nerve stimulation of the guinea-pig bladder. *British Journal of Pharmacology and Chemotherapy*, **25**, 288-294.

COOPER, J. R., BLOOM, F. E. and ROTH, R. H. (1974). *The Biochemical Basis of Neuropharmacology*, 2nd ed., New York: Oxford University Press, p. 85.

DIXON, J. S. and GOSLING, J. A. (1974). The distribution of noradrenergic nerves and small intensely fluorescent (SIF) cells in the cat urinary bladder. A light and electron microscope study. *Cell and Tissue Research*, **150**, 147-159.

DUMSDAY, B. (1971). Atropine-resistance of the urinary bladder innervation. *Journal of Pharmacy and Pharmacology*, **23**, 222-225.

ELBADAWI, A. and SCHENK, E. A. (1966). Dual innervation of the mammalian urinary bladder. A histochemical study of the distribution of cholinergic and adrenergic nerves. *American Journal of Anatomy*, **119**, 405-428.

FLETCHER, T. F., HAMMER, R. F. and BRADLEY, W. E. (1969). Nerve endings in the urinary bladder of the cat. *Journal of Comparative Neurology*, **136**, 1-19.

HENDERSON, V. E. and ROEPKE, M. H. (1934). The rôle of acetylcholine in bladder contractile mechanisms and in parasympathetic ganglia. *Journal of Pharmacology and Experimental Therapeutics*, **51**, 97-111.

HOYES, A. D. and BARBER, P. (1975). Ultrastructure of the corneal nerves in the rat. (In preparation.)

HOYES, A. D., BARBER, P. and MARTIN, B. G. H. (1975). Comparative ultrastructure of the nerves innervating the muscle of the body of the bladder. *Cell and Tissue Research*, **164**, 133-144.

HOYES, A. D., BOURNE, R. and MARTIN, B. G. H. (1974). Small dense-cored vesicles in the cholinergic nerve terminals of the rat bladder. *Journal of Anatomy*, **118**, 381.

——(1975*a*). Ultrastructure of the submucous nerves of the rat ureter. *Journal of Anatomy*, **119**, 123-132.

——(1975*b*). Ureteric vascular and muscle coat innervation in the rat. A quantitative ultrastructural study. *Investigative Urology* (in press).

HUKOVIĆ, S., RAND, M. J. and VANOV, S. (1965). Observations on an isolated, innervated preparation of rat urinary bladder. *British Journal of Pharmacology and Chemotherapy*, **24**, 178-188.

KARNOVSKY, M. J. (1965). A formaldehyde-glutaraldehyde fixative of high osmolarity for use in electron microscopy. *Journal of Cell Biology*, **27**, 137A-138A.

KATZ, Sir BERNARD and MILEDI, R. (1973). The effect of atropine on acetylcholine action at the neuromuscular junction. *Proceedings of the Royal Society, Series B*, **184**, 221-226.

KOELLE, G. B. (1961) A proposed dual neurohumoral role of acetylcholine: its functions at the pre- and post-synaptic sites. *Nature*, **190**, 208-211.

MCLELLAN, A. M. and GOODELL, H. (1943). Pain from the bladder, ureter, and kidney pelvis. *Research Publications of the Association for Nervous and Mental Disease*, **23**, 252-262.

RAEZER, D. M., WEIN, A. J., JACOBOWITZ, D. and CORRIERE, J. N., Jr. (1973). Autonomic innervation of canine urinary bladder: cholinergic and adrenergic contributions and interaction of sympathetic and parasympathetic nervous systems in bladder function. *Urology*, **2**, 211-221.

SCHULMAN, C. C., DUARTE-ESCALANTE, O. and BOYARSKY, S. (1972). The ureterovesical innervation: a new concept based on a histochemical study. *British Journal of Urology*, **44**, 698-712.

THAEMERT, J. C. (1963). The ultrastructure and disposition of vesiculated nerve processes in smooth muscle. *Journal of Cell Biology*, **16**, 361-377.

UEMURA, E., FLETCHER, T. F., DIRKS, V. A. and BRADLEY, W. E. (1973). Distribution of sacral afferent axons in cat urinary bladder. *American Journal of Anatomy*, **136**, 305-314.

UEMURA, E., FLETCHER, T. F. and BRADLEY, W. E. (1974). Distribution of lumbar afferent axons in muscle coat of cat urinary bladder. *American Journal of Anatomy*, **139**, 389-398.

YAMAUCHI, A. and BURNSTOCK, G. (1969). Post-natal development of the innervation of the mouse vas deferens. A fine structural study. *Journal of Anatomy*, **104**, 17-32.

The Authors

A. D. Hoyes, PhD, Reader, Department of Anatomy, St Mary's Hospital Medical School.
R. Bourne, MB, BS, Surgical Registrar, Queen Mary's Hospital, Roehampton.
B. G. H. Martin, Technician, Department of Anatomy, St Mary's Hospital Medical School.

Address for correspondence: Dr A. D. Hoyes, Department of Anatomy, St Mary's Hospital Medical School, Paddington, London W2 1PG.

British Journal of Urology (1976), **48**, 54 ©

Short Case Report

Recurrent Spontaneous Rupture of the Urinary Bladder

Pelvic trauma (Wheeler, 1972) and neuromuscular inco-ordination (Bliss, 1964) predispose to this rare condition. It has not been reported following bladder surgery.

Case Report

A woman aged 39 years had sudden onset of severe low abdominal pain and passed clear urine afterwards. Her abdomen was distended, rigid, with generalised tenderness. An IVP and retrograde cystogram showed a normal bladder outline. At laparotomy urine had leaked from a small perforation in the thin-walled scarred bladder fundus. This was excised and closed around a de Pezzer catheter. The peritoneal cavity was irrigated with Noxytiolin and drained; a Foley catheter drained the bladder. Prophylactic ampicillin was given. After catheter removal she was discharged on the 12th day with sterile urine and a well-healed abdomen.

15 years previously the upper loculus of a large bilocular bladder had been excised and 7 years later she had a spontaneous rupture of the bladder with clinical and operative findings identical to those in the recent episode.

Comment

Retrograde cystography in rupture of the bladder usually shows extravasation (O'Donoghue, 1973) but was unhelpful in this case. Early laparotomy, peritoneal cleansing, excision of scar tissue at the bladder fundus, which predisposed to the recurrent rupture, closure, drainage and antibacterial prophylaxis are the principal features of management of this condition.

F. R. JACKAMAN
St George's Hospital, London S.W.1.

References

BLISS, B. P., CLARK, W. G. B. and SAUNDERS, M. (1964). Recurring spontaneous rupture of the urinary bladder following subarachnoid haemorrhages. *British Journal of Surgery*, **51**, 446-448.

O'DONOGHUE, E. P. N., CHISHOLM, G. D. and SHACKMAN, R. (1973). Urinary fistulae after renal transplantation. *British Journal of Urology*, **45**, 28-33.

WHEELER, M. H. (1972). Recurrent spontaneous rupture of the urinary bladder. *British Journal of Surgery*, **59**, 938-984.

British Journal of Urology (1976), **48**, 55-59 ©

Single Dose Intravesical Thiotepa as an Adjuvant to Cystodiathermy in the Treatment of Transitional Cell Bladder Carcinoma

K. G. BURNAND, P. J. R. BOYD, M. E. MAYO, K. E. D. SHUTTLEWORTH and R. W. LLOYD-DAVIES
Department of Urology, St Thomas's Hospital, London

Tumour cell implantation is widely believed to be a factor in the aetiology of multiple urothelial tumours (Kirwin, 1943; Hinman, 1960; Boyd and Burnand, 1974). If implantation is a factor and if the number of tumour cells floating free within the bladder is increased as a result of cystodiathermy, then the destruction of these cells should reduce the incidence of recurrent tumour formation.

This paper reports a prospective randomised trial in which the cytotoxic agent thiotepa (triethylene thio-phosphoramide) was introduced into the bladder immediately after cystodiathermy. Control patients were treated by cystodiathermy alone and tumour recurrence was compared in the 2 groups.

Methods

A total of 51 patients were studied, 19 in the group treated with thiotepa and 32 in the control group. There were 16 men and 3 women in the thiotepa group and 27 men and 5 women in the control group. The mean age of thiotepa group patients was 60·5 years and the mean age of patients in the control group was 61·8 years.

Admission to the trial was allowed only after cystoscopy, panendoscopy and bimanual pelvic examination had been performed under general anaesthetic by an experienced endoscopist. All patients had tumours that were judged clinically to be limited to the mucosa or submucosa and thought suitable for treatment by endoscopic loop resection or fulguration. Biopsies were taken at this initial examination and subsequent histology confirmed that all these primary tumours were well differentiated and had not invaded muscle. Allocation to control or thiotepa groups was made in the operating theatre when the initial fulguration and resection had been completed and while the patient was still anaesthetised. Selection was made by spinning a coin.

Patients in the thiotepa group had a self-retaining balloon catheter passed and 90 mg thiotepa in 100 ml sterile water instilled into the bladder with a syringe. The catheter was spigotted and the patient transferred to the recovery room lying in the left lateral position. After 15 min the patient was turned to the right lateral position and after a further 15 min the bladder was emptied and the catheter removed. This procedure was repeated whenever a patient in the thiotepa group was found to have a recurrence at follow-up cystoscopy. If no recurrence was seen, no action was taken beyond the cystoscopy, panendoscopy and bimanual examination.

Patients in the control group were treated only by endoscopic fulguration or loop resection.

The site of tumours seen both at the initial assessment and on follow-up cystoscopy was charted on standard diagrams of the bladder. In assessing the results, tumour was labelled recurrent only if seen at a site previously clear of tumour. Tumour seen at the same site on successive cystoscopies was labelled residual tumour. To avoid employing the concept of subdivision of a recurrence which results from the use of a conventional recurrence rate, the frequency of tumour recurrence is expressed as the theoretical average time taken in months to develop a single recurrence. This value is calculated by dividing the number of months during which the patient has been kept under review by the number of recurrences seen during that time.

Patients were withdrawn from the trial for one or more of the following reasons:

1. If the tumour on follow-up assessment was thought to have spread beyond the mucosa
2. If repeat biopsy taken at follow-up cystoscopy showed any change in the histological pattern
3. If any treatment other than endoscopic resection and fulguration (with or without adjuvant thiotepa) was thought to be necessary.

The 51 patients were all followed regularly by check cystoscopy for between 2 and 5 years. 2 patients were withdrawn when their tumours became invasive and 5 patients were transferred from the control to the thiotepa group when it became apparent that cystodiathermy was being needed at increasingly frequent intervals in order to control their tumours. These 5 "transferred" patients are considered as a separate group. In formulating the results all 7 patients are included within the control group up to the time at which they were withdrawn or transferred.

Results

Table I indicates the site of primary tumour. The distribution between different sites is broadly similar in the two groups and it may be noted that the number of primary tumours involving the vault of the bladder is low in both groups.

The site of recurrent tumour is shown in Table II. There are important differences between the

Table I

Site of Primary Tumour

Site	Control group	Thiotepa group
Vault alone	1	0
Base or walls alone	21	11
Multiple tumours involving vault	1	1
Multiple tumours not involving vault	9	7
Total	32	19

Table II

Site of Recurrent Tumour

Site	Control group	Thiotepa group
Vault alone	7	0
Base or walls alone	2	2
Multiple involving vault	22	9
Multiple not involving vault	0	0
No recurrence	1	8
Total	32	19

Table III

Theoretical Average Time to Develop One Recurrence

Control group (31 patients)	2·66 months
Thiotepa group (11 patients)	2·20 months
"Transferred" group before adjuvant thiotepa (5 patients)	1·58 months
"Transferred" group after adjuvant thiotepa (4 patients)	0·97 months

2 groups of patients. 8 patients in the group of 19 treated with thiotepa remained free of recurrence, whereas only 1 of the 32 patients in the control group remained recurrence free. This difference is highly significant—$\chi^2 = 11{\cdot}8$ $P < 0{\cdot}001$. The distribution of recurrent tumour is also altered. None of the patients in the group treated with thiotepa developed recurrences limited to the vault of the bladder but 7 of the patients in the control group developed recurrences only at this site. This difference is also highly significant—$\chi^2 = 12{\cdot}8$ $P < 0{\cdot}0005$. Table III shows the frequency of recurrence in those patients who developed recurrent tumour and there is no significant difference between the two main groups. The group of 5 "transferred" patients is similar in behaviour to the main thiotepa group in that 1 patient remained free from any further recurrent tumour after a single dose of adjuvant thiotepa and the remaining 4 patients continued to develop tumour recurrences at an undiminished rate despite adjuvant thiotepa.

Discussion

Thiotepa (tri-ethylene thio-phosphoramide) is a polyfunctional alkylating agent which is believed to exert its cytotoxic effect through indirect interference with nucleic acid synthesis. The effectiveness of intravesical thiotepa is attributed to the relatively low level of mitotic activity of normal urothelium compared with the higher level of mitosis in urothelial tumours. Since the preliminary reports of Bateman (1955) and of Jones and Swinney (1961), a large number of workers have published their findings (Veenema *et al.*, 1969; Drew and Marshall, 1968; Zingg and Sulmoni, 1972). It is now generally accepted that intravesical thiotepa is of value in the treatment of well or moderately differentiated superficial bladder tumours but that it is of little or no benefit once the tumour has invaded muscle. Westcott (1966) and Veenema *et al.* (1969) have reported favourable results using intravesical thiotepa prophylactically and it has been suggested that the beneficial effects result from the destruction of microscopic foci of tumour (Veenema *et al.*, 1969).

The complications of intravesical thiotepa have prevented its wider acceptance. Bone marrow depression resulting from absorption into the systemic circulation may prove fatal (Bruce and Edgcomb, 1967; Watkins, Kozak and Flanagan, 1967) and symptoms of urethrovesical irritation may be troublesome (Jones and Swinney, 1961; Veenema *et al.*, 1969). Intravesical thiotepa is usually administered as a course of 4 to 6 treatments. 60 mg thiotepa is introduced at each treatment for 60 to 90 min and this is repeated at daily or weekly intervals. It seems likely that the repetitive nature of this method increases the likelihood of developing complications.

The single dose technique described in this paper in which 90 mg of thiotepa is administered intravesically for only 30 minutes reduces both the chance of significant systemic absorption and of urethrovesical irritation. Only one transient postoperative reduction of WBC was observed and there were no complaints of undue postoperative discomfort from patients in either group. Single dose techniques have been described by other authors (Westcott, 1966; Hinman, 1956; Crassweller, Ley and Ranking, 1968) but no results with thiotepa have so far been reported. This technique is simple, relatively free from complications, does not significantly prolong conventional methods of treatment and causes minimal discomfort and inconvenience to the patient.

Although the numbers in this series are small, 2 important facts emerge. First, the number of patients who remained free from recurrent tumour was significantly greater in the thiotepa group than in the control group. Secondly, the continued use of adjuvant thiotepa in patients who developed recurrent tumour did not diminish the frequency of recurrence. It follows that in this study satisfactory results appear only to follow the initial treatment with adjuvant thiotepa. This fact could be explained if implanting tumour cells were destroyed in those patients who remained free of recurrent tumour, while recurrences in other patients arose from spontaneous change in an unstable epithelium.

The method of action of thiotepa when given as an adjuvant to cystodiathermy is uncertain. It may be effective through its action on microscopic established tumours that are too small to be seen cystoscopically or possibly through the destruction of implanting tumour cells. The high incidence of vault recurrence in the control group of patients has previously been reported (Boyd and Burnand, 1974), and it is suggested that this finding is best explained by tumour cell implantation. The patients in the thiotepa group have significantly fewer pure vault recurrences than the patients in the control group, and this difference may result from a reduction in the number of implanting cells after treatment with intravesical thiotepa.

During this study no patient was followed for more than 5 years, and the response of a tumour appearing after a 5-year interval to further adjuvant thiotepa has not been assessed.

Summary

Tumour cell implantation may be a factor in the aetiology of recurrent well-differentiated superficial bladder tumours.

A prospective trial is reported in which single dose intravesical thiotepa was administered to a group of randomly selected patients immediately after cystodiathermy. A control group of patients was treated by cystodiathermy alone and tumour recurrence in the 2 groups was compared.

Significantly fewer patients in the thiotepa-treated group developed recurrent tumour and there was also a significantly reduced incidence of pure vault recurrence in this group.

The beneficial effects of adjuvant thiotepa were apparent after 1 treatment. In this series of patients no benefit resulted from the continued use of adjuvant thiotepa once a patient developed a recurrent tumour.

References

BATEMAN, J. C. (1955). Chemotherapy of solid tumours with triethylene thiophosphoramide. *New England Journal of Medicine*, **252**, 879-887.

BOYD, P. J. R. and BURNAND, K. G. (1974). Site of bladder-tumour recurrence. *Lancet*, **2**, 1290-1292.

BRUCE, D. W. and EDGCOMB, J. H. (1967). Pancytopenia and generalized sepsis following treatment of cancer of the bladder with instillations of triethylene thiophosphoramide. *Journal of Urology*, **97**, 482-485.

CRASSWELLER, P. O., LEY, D. C. H. and RANKING, G. N. (1968). The use of nitrogen mustard for prevention of bladder tumor recurrence. *Journal of Urology*, **100**, 21-23.

DREW, J. E. and MARSHALL, V. F. (1968). The effects of topical thiotepa on the recurrence rate of superficial bladder cancers. *Journal of Urology*, **99**, 740-743.

HINMAN, F. (1956). Recurrence of bladder tumors by surgical implantation. *Journal of Urology*, **75**, 695-696.

—— (1960). The recurrence of bladder tumors. *Journal of Urology*, **83**, 294-300.

JONES, H. C. and SWINNEY, J. (1961). Thiotepa in the treatment of tumours of the bladder. *Lancet*, **2**, 615-618.

KIRWIN, T. J. (1943). Papillomatosis of the bladder: new conceptions of etiology and treatment. *Journal of Urology*, **49**, 1-13.

Veenema, R. J., Dean, A. L., Uson, A. C., Roberts, M. and Longo, F. (1969). Thiotepa bladder instillations: therapy and prophylaxis for superficial bladder tumors. *Journal of Urology*, **101**, 711-715.
Watkins, W. E., Kozak, J. A. and Flanagan, M. J. (1967). Severe pancytopenia associated with the use of intravesical thiotepa. *Journal of Urology*, **98**, 470-471.
Wescott, J. W. (1966). The prophylactic use of thiotepa in transitional cell carcinoma of the bladder. *Journal of Urology*, **96**, 913-918.
Zingg, E. and Sulmoni, A. (1972). Chemotherapy in superficial neoplasms of the bladder. *South African Medical Journal*, **46**, 916-917.

The Authors

K. G. Burnand, FRCS, Research Fellow, Department of Surgery.
P. J. R. Boyd, FRCS, Renal Research Fellow (now Lecturer in Urology, Charing Cross Hospital).
M. E. Mayo, MS, FRCS, Senior Lecturer, Institute of Urology.
K. E. D. Shuttleworth, MS, FRCS, Consultant Urologist.
R. W. Lloyd-Davies, MS, FRCS, Consultant Urologist.

Requests for reprints to K. G. Burnand, Department of Urology, St Thomas's Hospital, London S.E.1.

British Journal of Urology (1976), **48**, 60 ©

Short Case Report

Recurrent Transitional Cell Carcinoma complicating Ileal Conduit

Case History

A 56-year-old male with a 17-year history of papillary bladder tumours had a total cystectomy performed in 1971 with the formation of an ileal conduit. 9 months postoperatively he developed a left perinephric abscess which was drained. Left loin pain and swelling recurred 6 months later and percutaneous aspiration of the presumed perinephric abscess was attempted. Blood was obtained but no pus.

Intravenous urography showed no excretion on the left and a right hydronephrosis. Retrograde ileography demonstrated an irregular filling defect and absence of ileo-ureteric reflux (Fig.). Left nephro-ureterectomy with revision of the conduit confirmed the diagnosis of recurrent transitional cell carcinoma involving the renal pelvis and full length of the left ureter, and also obstructing the right ureter by involvement of the adjacent ileum.

Comment

Ileo-ureteric reflux is a normal finding on retrograde ileography (Campbell, Oliver and McKay, 1965). This simple examination therefore permits visualisation of the whole urinary tract, which can be difficult to attain by other routes in patients with ileal urinary diversions. Absence of ileo-urereti c reflux is a significant finding as is the late development of a hydronephrosis (Bowles, Cordonnier and Parsons, 1964). Recurrent tumours complicating ileal conduits are rare. 2 have been described by Soloway *et al.* (1972) in a study of the value of exfoliative cytology in the diagnosis of recurrence in the patient with an ileal urinary diversion.

D. M. Allan
St Peters Hospital, Chertsey, Surrey

Present address: *Radiology Department, Radcliffe Infirmary, Oxford.*

References

Bowles, W. T., Cordonnier, J. J. and Parsons, R. P. (1964). Treatment of late uretero-ileal stenosis following ileal segment urinary diversion. *Journal of Urology*, **92**, 627-634.

Campbell, J. E., Oliver, J. A. and McKay, D. E. (1965). Dynamics of ileal conduits. *Radiology*, **72**, 211-216.

Soloway, M. S., Myers, G. H., Burdick, J. F. and Malmgren, R. A. (1972). Ileal conduit exfoliative cytology in the diagnosis of recurrent carcinoma. *Journal of Urology*, **107**, 835-839.

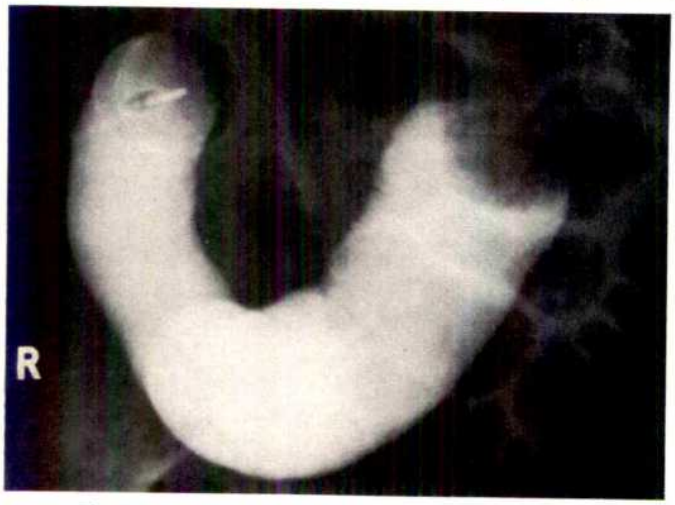


Fig. Retrograde ileogram showing polypoid filling defect.

British Journal of Urology (1976), **48**, 61-71 ©

Studies on the Chemical Nature of Urinary Chemiluminescence

G. ALAN ROSE
St Peters Hospitals and Institute of Urology, London

The hypothesis that chemicals might act as carcinogenic agents by dint of ability to exhibit chemiluminescence was put forward by Anderson (1947) and extended by Steele (1966). It was not possible at first to test this hypothesis because of restrictions imposed by existing instruments but Schlegel *et al.* (1969*a*) were able to show some correlation, albeit it a weak one, between urinary chemiluminescence and carcinoma of the bladder. They thought that there was higher chemiluminescence in urine from smokers than from non-smokers and even higher chemiluminescence in urine from patients with cancer of the bladder. These results were confirmed and extended by Schlegel *et al.* (1969*b*) and by Rose and Wallace (1973).

Objectives

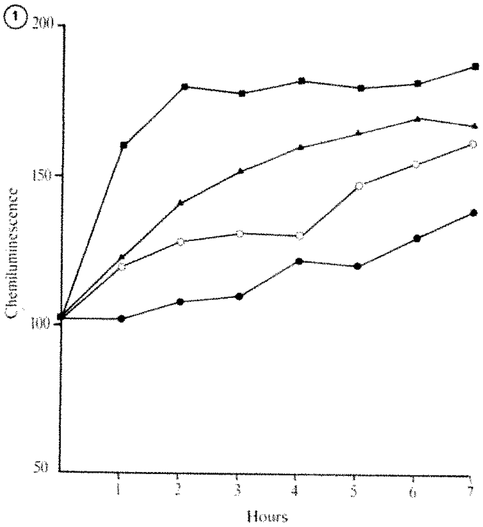
Practically nothing has previously been reported on the nature of the chemiluminescent material in urine. The only clue has been the unsupported comment of Rose and Wallace (1973) that urinary chemiluminescence would dialyse through Cellophane tubing. It was therefore decided to try to learn more of the chemical nature of urinary chemiluminescence and also of the chemiluminescence of chemicals which might conceivably be responsible for the phenomenon in urine. The work to be described falls into several categories. Firstly, it became apparent that acid treatment of urine led to an enormous increase in chemiluminescence and an attempt was therefore made to study the conditions under which this occurred. Secondly, further studies on molecular size of the chemicals causing urinary chemiluminescence were performed, using ultrafiltration techniques. Thirdly, attempts were made to isolate the chemiluminescent material by sephadex columns and the results are reported. Fourthly, the chemiluminescence of a number of chemicals thought to be relevant in the context of carcinoma of the bladder, tobacco smoking and chemical carcinogens, has been studied.

Methods

Chemiluminescence was measured by the Du Pont luminescence biometer as described by Schlegel *et al.* (1969*b*) and by Rose and Wallace (1973). The technique with this instrument was that of Rose and Wallace (1973). The normal human urine samples were obtained fresh from laboratory workers in the hospital. All measurements and procedures were performed without delay and normally on the same day. Occasionally, this was obviously not possible, as when hydrolysed urine was allowed to stand overnight, or was subjected to chromatography overnight. The dog urines were obtained by catheterisation and frozen solid until the measurements were made some weeks later. Chemiluminescence was then measured immediately after thawing. Some of these dogs had been treated with alpha- and/or beta-naphthylamine but there were also some control dogs who had received no chemicals. Because haemoglobin is known to cause chemiluminescence (Rose and Wallace, 1973) all urine samples, whether human or animal, were tested for haemoglobin chemically, and rejected if haemoglobin was detected.

The creatinine content of all urine samples was measured by Auto-Analyser using the standard method and the chemiluminescence corrected to standard creatinine concentration (Rose and Wallace, 1973).

Ultrafiltration studies were performed with a motorised syringe pump and an Amicon ultrafiltration unit as described for the ultrafiltration of plasma by Rose (1972). The pore size of the ultrafilter corresponded to a molecular weight of 500.



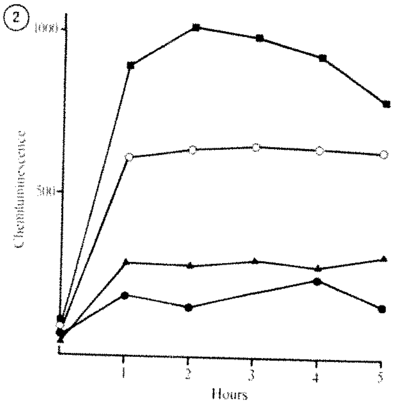
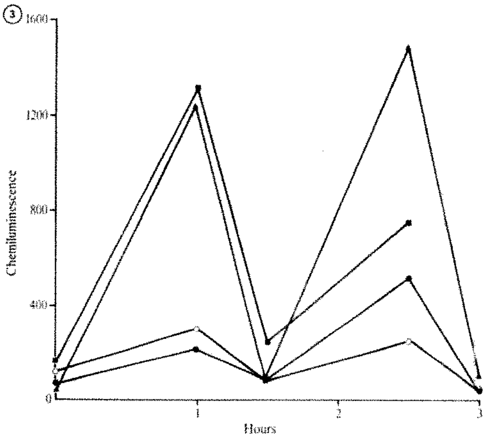


Fig. 1. A single sample of urine of pH 6·9 was split into 4 fractions and each was heated for 7 hours at the temperatures indicated. The chemiluminescence of each fraction was measured at hourly intervals. ●—● 20°C; ○—○ 40°C; ▲—▲ 70°C; ■—■ 100°C.

Fig. 2. Samples of urine of neutral pH from 4 normal subjects were boiled continuously for 5 hours under reflux condenser and the chemiluminescence measured at hourly intervals.



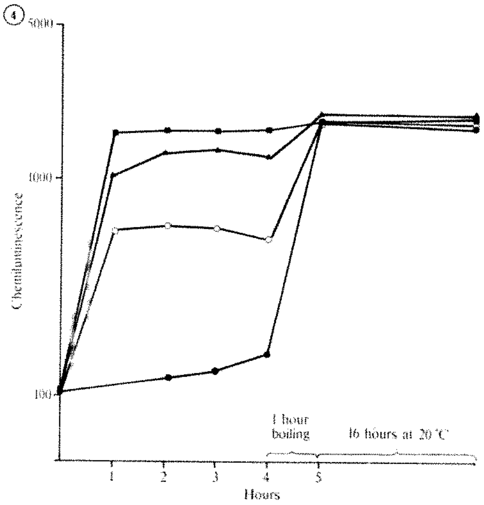


Fig. 3. Samples of urine of neutral pH from 4 normal subjects were boiled from hours 0-1, left to cool from hours 1-1½, boiled again from hours 1½-2½ and left to cool again from hours 2½-3. Note the rapid decay in chemiluminescence on cooling.

Fig. 4. A single sample of normal urine was brought to pH 1 and split into 4 fractions which were then heated at various temperatures for 4 hours. Then, each fraction was boiled under reflux condenser for 1 hour and finally left to cool and stand overnight at 20°C. ●—● 20°C; ○—○ 38°C; ▲—▲ 79°C; ■—■ 100°C.

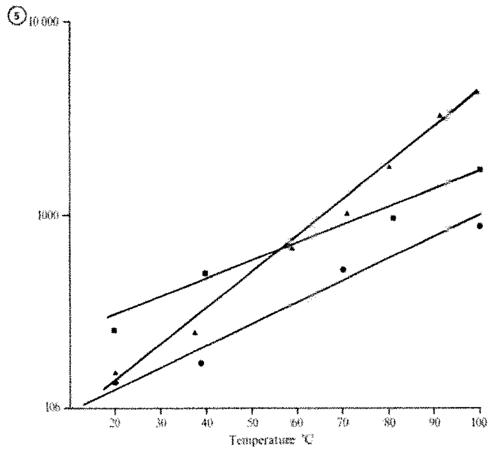


Fig. 5. Each of 3 samples of normal urine was brought to pH 1 and then different portions heated for 1 hour at the various temperatures shown.

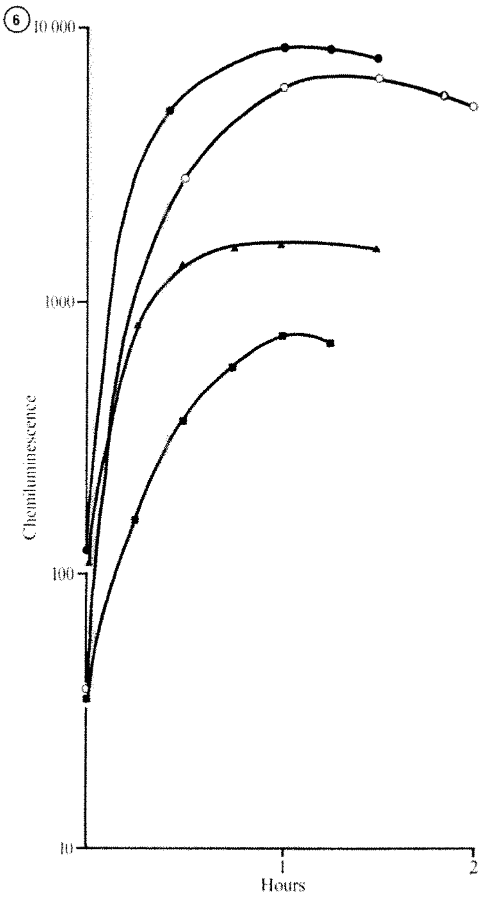


Fig. 6. Each of 4 samples of normal urine was brought to pH 1 and then boiled for up to 2 hours. Samples were withdrawn for measurement of chemiluminescence at the times shown.

Results and Comments

Effect of Heating Urine at Neutral pH

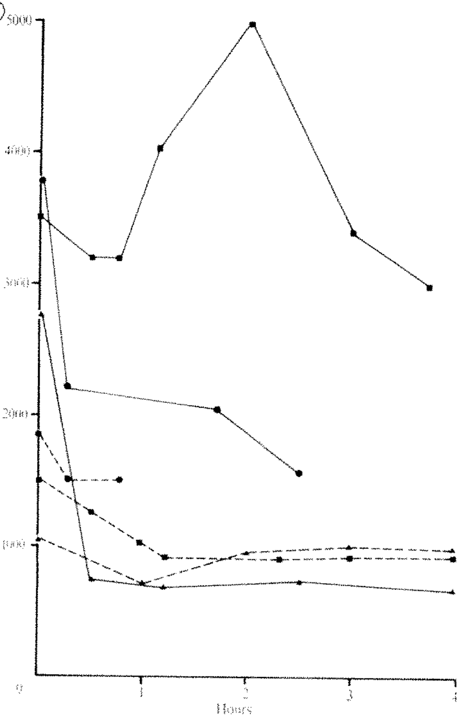
Figure 1 shows that when a single sample of urine was heated at neutral pH and at various temperatures and for up to 7 hours, the chemiluminescence could be increased by a factor of about 1·3-1·8. Figure 2 shows that when 4 different samples of normal urine were subjected to continuous boiling for up to 5 hours at neutral pH the urinary chemiluminescence rose by about 4 to 100-fold. These rises in chemiluminescence were only consistently observed, however, if the measurements were made immediately after the period of heating had ended. Therefore, samples were removed after the specified periods of heating, rapidly cooled and the chemiluminescence immediately measured. Figure 3 shows that 30 min. after a 1-hour period of boiling, the urinary chemiluminescence had dropped back nearly to the initial figure, and that the whole cycle could be repeated.

These results seem to suggest that heating the urine causes some molecular activation of the chemiluminescence which fades away after cooling.

Effect of Heating Urine at pH 1

Much larger rises in urinary chemiluminescence were achieved by first bringing the urine samples to pH 1. Figure 4 shows the results obtained when a single sample of normal urine was acidified to pH 1 with conc. HCl and then heated at different temperatures for up to 4 hours. Finally, each sample was boiled under reflux condenser for 1 hour and then allowed to stand overnight. When 3 different acidified urine samples were heated at different temperatures for 1 hour only, the rises in chemiluminescence were as shown in Figure 5. Figure 6 shows the effect

⑦



⑧

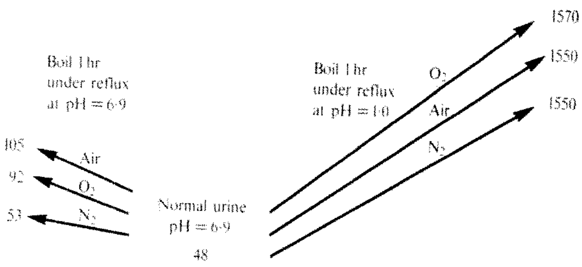


Fig. 7. Each of 6 samples of normal urine had been boiled for 90 minutes at pH 1 to give the chemiluminescence indicated at 0 hours. Each sample was then allowed to stand at room temperature for up to 4 hours. Note how the chemiluminescence decayed rapidly in 5 samples, whereas quite irregular and inexplicable changes occurred in the sixth.

Fig. 8. Diagram to show effect of atmosphere on changes in chemiluminescence on boiling a urine sample at neutral and at acid pH. Oxygen was not required for the rise in chemiluminescence of pH 1, but was required to give a rise at neutral pH.

of continuous boiling upon the urinary chemiluminescence of acidified urine. The overall rise was variable but was usually about 100-fold as shown in Figure 9 for both man and dogs.

If after boiling the urine at pH 1, it was allowed to stand at room temperature the stability of the very large chemiluminescence was rather variable. Sometimes it remained at a constant high level as shown in Figure 4 but sometimes decayed rather rapidly as shown in 5 out of 6 samples in Figure 7. No explanation for these variations could be found and the decay in chemiluminescence could not be related to exposure to light.

There seemed to be two possible explanations for the remarkable rises in chemiluminescence produced on the boiling of urine at pH 1. Additional chemiluminescent material might be generated or activated from an inert chemical either by oxygenation or hydrolysis. To distinguish between these possibilities the boiling experiments were repeated under atmospheres of air, oxygen and nitrogen.

Effect of Atmosphere on Chemiluminescence of Heated Urine

Samples of urine were heated under reflux condenser, either with or without previous acidification to pH 1, using an atmosphere of air, nitrogen or oxygen. The results of such an experiment are shown in Figure 8 and it is clear that the specific atmosphere did not affect the results when at pH 1, whereas at neutral pH oxygen was required to induce a rise in chemiluminescence.

These results suggest that the molecular activation process postulated to explain the rise in chemiluminescence at neutral pH requires oxygen, whereas the large rises in chemiluminescence at pH 1 are independent of oxygen and therefore likely to be due to hydrolysis.

Enzyme Hydrolysis of Urine

Such hydrolysis may take the form either of opening the ring of a cyclic compound, or the splitting of a conjugating compound such as glucuronic acid or sulphate. To distinguish between these possibilities the effect on urine of certain enzymes was studied. Figure 10 shows the effect on human urine at pH 5 of the enzymes sulphatase and beta glucuronidase. Each enzyme was allowed to act on a different aliquot of urine for up to 4 hours, after which it was acidified to pH 1 and boiled under reflux condenser for 90 min. The sulphatase raised the chemiluminescence by a factor of 2·5, the beta glucuronidase by a factor of 21. Subsequent acidification and boiling, however, yielded a further and much larger rise in chemiluminescence to a total of 180-fold.

Table I

Effect of Ultrafiltration upon Urinary Chemiluminescence

	pH	Untreated urine	Ultrafiltrate	Residual Urine after UF	Ultrafiltrate and residue combined
	Unhydrolysed				
1	5·0	170	210	135	173
	6·0	185	220	140	185
	7·0	168	174	155	170
2	5·0	106	160	71	110
	6·0	140	180	110	145
	7·0	200	260	140	210
	Acid hydrolysed at pH 1, pH adjusted before UF				
1	5·0	3100	2000	4600	3200
	6·0	1160	900	1380	1040
	7·2	1040	800	1100	980

The chemiluminescence was measured on 2 unhydrolysed and upon 1 hydrolysed samples of urine before and after ultrafiltration through Amicon filter UM-05 with molecular weight cut off at 500.

Table II

Effect of Ultrafiltration upon Urinary Chemiluminescence

	Unhydrolysed urine			Hydrolysed urine	
pH	Pre U/F	U/F	Hydrolysed U/F of unhydrolysed urine	Pre U/F	U/F
5·9	61	160	18,500	22,000	18,000
6·9	135	140	6,100	8,000	15,000
6·2	160	250	22,000	22,500	19,000
5·4	39	59	210	200	
8·9	92	105	5,900	5,250	

The chemiluminescence was measured on 5 samples of urine both before and after acid hydrolysis at pH 1 for 90 min. Ultrafiltration was through Amicon filter (see Table I). The middle column shows the chemiluminescence obtained after the UF from unhydrolysed urine had been submitted to acid hydrolysis.

It is therefore concluded that in this urinary sample, and it was typical of others also tested, only 0·6% of the chemiluminescence was conjugated with sulphate, 1% with beta glucuronic acid and no less than 85% was combined in some other inert form or forms.

Ultrafiltration Studies

Results of ultrafiltration studies are shown in Tables I and II. When untreated urine was tested it was found that the chemiluminescence of the ultrafiltrate was always higher than that of the original urine, while the chemiluminescence in the urine remaining proximal to the filter correspondingly decreased. On recombing the ultrafiltrate with the unfiltered urine the original chemiluminescence was obtained. These changes were attributed to the corresponding colour changes. Thus, the ultrafiltrate was always much paler than the original urine while

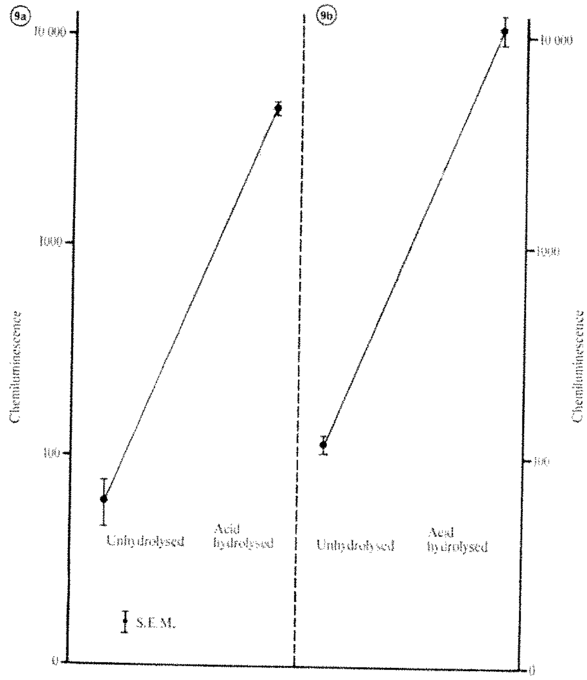


Fig. 9. Mean and SEM for urinary chemiluminescence of samples of urine before and after acid hydrolysis. A, 9 samples of normal human urine. B, 29 samples of dog urine. Left, unhydrolysed; Right, after hydrolysis.

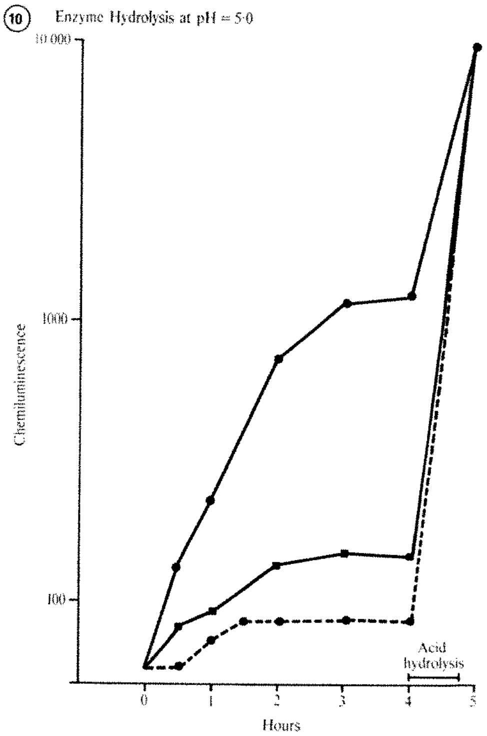


Fig. 10. A single sample of urine was brought to pH 5 and left to stand at 37°C for 4 hours either alone (●... ●) or with sulphatase (■—■) or with beta-glucuronidase (●—●). At the end of this period each sample was brought to pH 1 and boiled for 1 hour under reflux condenser.

the unfiltered urine correspondingly darkened, presumably because some of the urinary pigments could not pass the ultrafilter. Similar changes were not seen in the case of acid hydrolysed urine samples in Table II presumably because although these were darker in colour they were diluted 100 to 1000 times before measuring chemiluminescence, so diluting out the colour.

Allowing for these factors, the Tables clearly show firstly that urinary chemiluminescence is freely ultrafiltered both before and after hydrolysis and secondly that the precursor of chemiluminescence present in unhydrolysed urine also ultrafiltered freely through the filters used. Both the chemiluminescent material and inert precursors must therefore be below molecular weight of 500.

Separation of Chemiluminescence on Sephadex Columns

It is reasonable to ask whether the chemiluminescence arising on boiling the urine with acid is due to the same molecular species as that which causes chemiluminescence in untreated urine. Some evidence for supposing that the species are the same is proved by the separation experiments performed by sephadex chromatography. Since these experiments had to run overnight, it was desirable to try to prevent spontaneous decay of chemiluminescence and therefore the eluting fluid had previously been bubbled with nitrogen in order to deoxygenate it. The results of these experiments are shown in Figures 11 and 12. It can be seen that in both fresh and acid-boiled urine, 2 peaks of chemiluminescence emerged from the column ahead of substances which showed ultraviolet absorption. On several occasions it was found possible to evaporate to dryness in vacuo the fractions showing the peak chemiluminescence and obtain a white powder with intense chemiluminescence. However, the weight of the powder was rather high. For example, 25 ml of acid-boiled urine yielded 59 mg of white powder and it seems likely that the main constituent must have been something other than chemiluminescent material. However, the whole of the powder and the chemiluminescence ultrafiltered freely and therefore consisted of chemicals of low molecular weight.

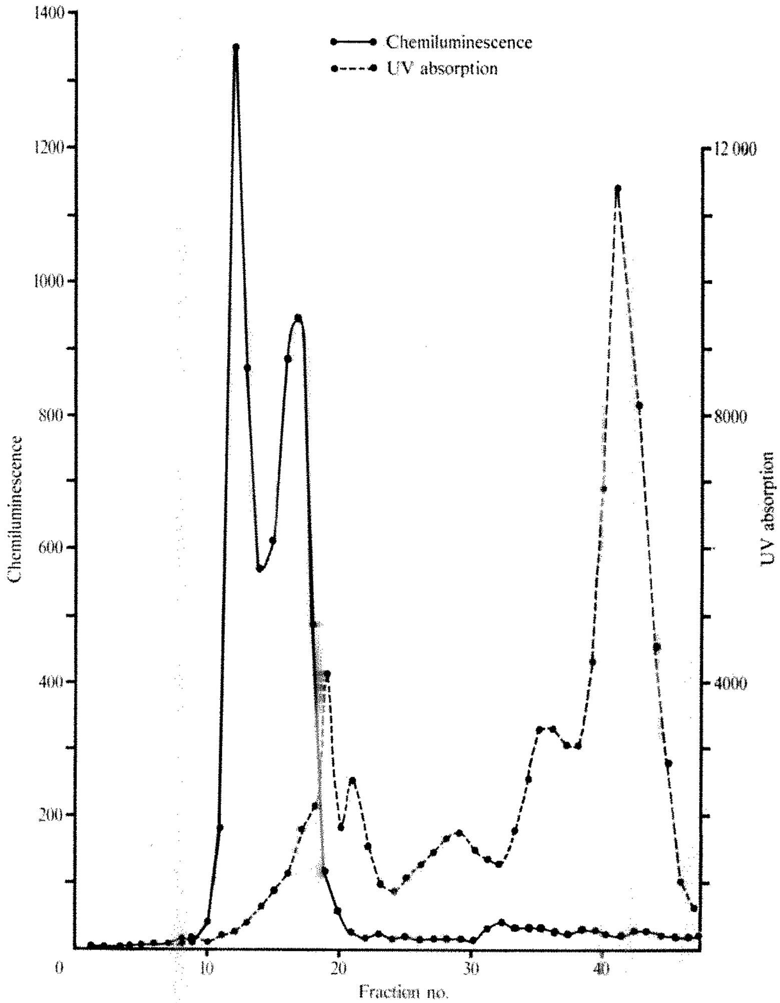


Fig. 11. 20 ml of normal urine was applied to a 3 times 33 centimetre column of sephadex G10 and eluted overnight at 54 ml per hour with distilled water acidified to pH 2·8 with HCl and bubbled with nitrogen. The volume of each fraction was 10 ml. ●— ● chemiluminescence; ●--- ● ultraviolet absorption.

Chemiluminescence of Various Chemicals

The relative chemiluminescence of various chemicals when dissolved in water as a 1% solution are shown in Table III.

Discussion

The results of studies of chemiluminescence reported here extended over several years and could not invariably be reproduced. There were unexplained deviations at times for reasons which were not always apparent. Some of the earlier deviations were later explained by the sensitivity to pH and temperature that was subsequently revealed. There are undoubtedly, however, other factors which affect urinary chemiluminescence that we still do not understand. The results

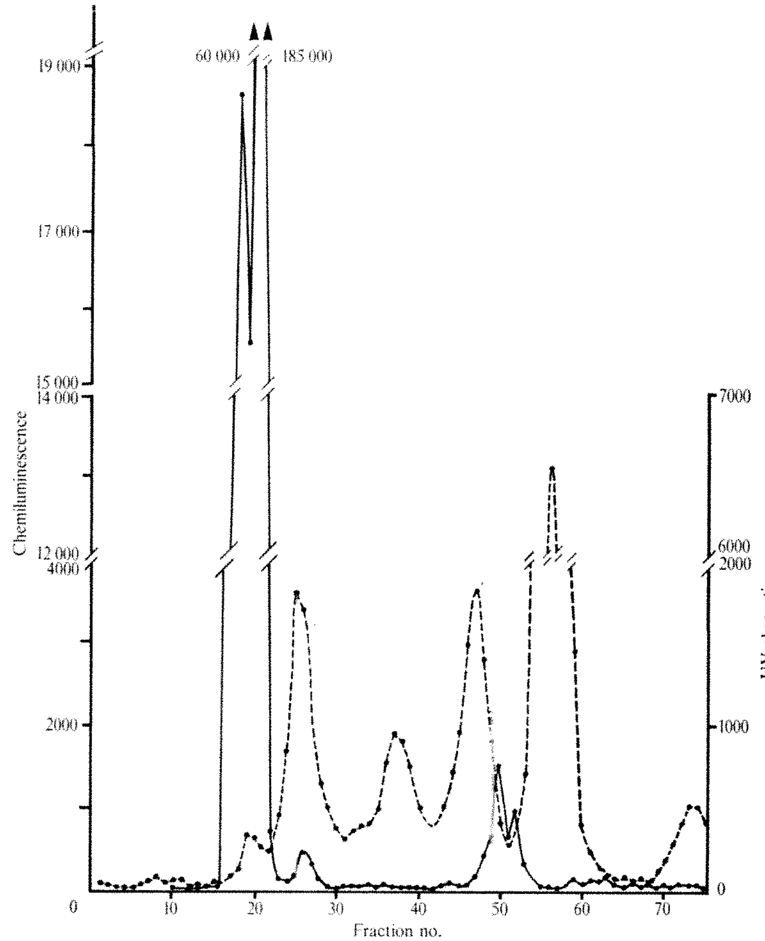


Fig. 12. A normal urine sample was acidified to pH 1 and boiled under reflux condenser for 90 min. The chemiluminescence rose from 52 to 84,500. 10 ml was then applied to a 3 times 75 centimeter column of sephadex G10 and eluted as described for Fig. 11. The 2 main peaks of chemiluminescence accounted for 82% of the initial chemiluminescence of the acid hydrolysed urine. ●—● chemiluminescence; ●---● ultraviolet absorption.

given here are representative of the large amount of work performed and the examples given indicate what was generally observed despite the occasional striking exceptions.

The data seems to suggest that urinary chemiluminescence may be increased by at least 2 mechanisms. Firstly, heating at neutral pH leads to a shortlived and small increase which is dependent upon oxygen and may be due to a molecular activation process. Secondly, heating at pH 1 leads to a large increase which is more permanent, cannot be induced again by a second heating and is independent of oxygen. The possibility that urinary chemiluminescene stems from a relatively large amount of inactive precursor is a new concept now put forward to explain the enormous rise in chemiluminescence which was consistently found on boiling urine at pH 1. This hypothesis also seems to offer an explanation for the fact that urinary chemiluminescence is surprisingly constant at room temperature (Rose and Wallace, 1973) or may even increase on standing (Fig. 1) whereas one might expect that chemiluminescence, like radioactivity, would steadily decay with time. It might be supposed that at room temperature and at neutral pH the

Table III

Chemiluminescence of Various Compounds when in 1% Solution

Compound	Chemiluminescence
[1] 2-naphthylhydroxylamine	1800
[2] Parasorbic acid	480
[3] 2-amino-1-naphthyl dihydrogen phosphate	400
[1] 1-naphthylhydroxylamine	350
[3] Bis-(2-amino-1-naphthyl) hydrogen phosphate	320
[3] Indoxyl sulphate	150
[3] 2-Formamido-1-naphthyl sulphate	120
[3] 1-naphthylamine	100
[3] 2-amino-1-naphthyl sulphate	60
[4] Glucuronic acid lactone	25
[4] Glucuronic acid	20
[5] Kynurenic acid	26
[3] nitrosopyrrolidine	11
[4] Butyro-lactone	4
[3] Spermidine	2
[6] nitrosodimethylamine	6
[3] nitrosopiperidine	1
[7] dibutyl-nitrosamine	1
[3] nitrosomorpholine	0
[3] n-methyl-n-nitroso-aniline	0
[3] Bis-(p-nitrophenyl) hydrogen phosphate	0
[3] Bis-(2-amino-1-naphthyl) hydrogen phosphate pyridine salt	0
[3] 2-amino-1-naphthol	0
[3] 2-naphthylamine	0
[8] Hydroxylamine	0
[7] Methylnitroso urea	0
Thiamine	0
[3] P-OH-hippuric acid	0
[3] Spermine	0
[3] Hippuric acid	0
[8] Anthranilic acid	0
[3] N-hydroxy anthranilic acid	0
[3] 3-hydroxy anthranilic acid	0
[3] 5-hydroxy anthranilic acid	0
[8] Riboflavin	0
[3] Cotidine	0
[3] Nicotine	0
[5] Xanthurenic acid	0
[5] 3-OH Kynurenine	0
[6] Shikimic acid	0

Sources of various chemicals as follows: [1] Synthesised by method of Willstätter and Kübli (1908). [2] Given by BIBRA. [3] Given by Professor Boyland. [4] Bought from Sigma Chemical Company. [5] Bought from Koch Light Laboratory Limited, Bucks. [6] Bought from Ralph Emmanuel Limited, Wembley. [7] Given by Dr. M. Hicks, Middlesex Hospital. [7] Bought from BDH Biochemicals, Poole, Dorset.

rate of decay of chemiluminescence is matched, or more than matched, by spontaneous breakdown of the non-chemiluminescent precursor substance or substances.

The nature of the inert precursor of the chemiluminescent material is obviously of considerable interest. It has been shown by the ultrafiltration studies that both the chemiluminescent material and the precursors are of molecular weight below 500. Furthermore, while some of the chemiluminescence is apparently bound as inert sulphate and glucuronate, such compounds only account for a small part of the total inert precursors. The possibility exists that the activation of the main precursor may take the form of a ring-opening process.

The theory linking chemiluminescence with bladder cancer requires that there should be a chemical present in urine which causes both phenomena. Since bladder cancer is induced by tobacco smoking (Lockwood, 1961; Cole *et al.*, 1971) and by beta-naphthylamine (Case *et al.*, 1954) and possibly by tryptophane metabolites, it seemed reasonable to test the chemiluminescence of as many as possible of the chemicals involved in these processes. Table III shows that it was possible to find very little or no chemiluminescence in the various tryptophane metabolites that were tested and in particular both 3-hydroxykinurenine and 3-hydroxyanthranilic acid showed no chemiluminescence although each has been thought to be carcinogenic (Allen *et al.*, 1957). The list of other chemicals which did not chemiluminesce includes shikimic acid, the substance isolated from bracken fern by Evans and Osman (1974) and which they found to cause carcinoma of the stomach and leukaemia in mice but, perhaps significantly, not carcinoma of the bladder. 2-naphthylamine was also found to be non-chemiluminescent, in keeping with the fact that the carcinogenicity of naphthylamine is not due to the chemical itself but to its metabolites. Just which metabolites are responsible is still not entirely clear, but current workers favour the nitroso compounds and the hydroxylamines (Radomski *et al.*, 1971). It is therefore of great interest and possibly significant that 2-naphthylhydroxylamine is the most chemiluminescent substance in Table III. This observation provides a new link between bladder cancer and urinary chemiluminescence.

Summary

Studies on the nature of the chemicals responsible for urinary chemiluminescence have been carried out.

Urinary chemiluminescence can be increased slightly by sulphatase, more by glucuronidase but most of all by boiling for 1 hour at pH 1. It is suggested that most of the chemicals responsible for urinary chemiluminescence are bound as non-chemiluminescent precursors to sulphate, glucuronic acid and in other ways.

Both the chemiluminescent material and the inactive precursors are freely ultrafiltrable with molecular weights below 500.

A survey of various chemicals has revealed considerable chemiluminescence in certain metabolites of naphthylamines and known to cause bladder cancer but little or no chemoluminescence in the tryptophane metabolites that have been thought to cause bladder cancer.

I am grateful to Mrs H. Durbin for extensive technical assistance and to all those normal volunteers who donated samples of urine. The samples of dog urine were kindly obtained from Dr Purchase of ICI Industrial Hygiene Research Laboratories at Alderley Park, Cheshire. Professor Boyland gave much helpful advice and also certain valuable chemicals.

References

ALLEN, M. J., BOYLAND, E., DUKES, C. E., HORNING, E. S. and WATSON, G. J. (1957). Cancer of the urinary bladder induced in mice with metabolites of aromatic amines and tryptophan. *British Journal of Cancer*, **11**, 212-228.

ANDERSON, W. (1947). Physico-chemical aspects of chemical carcinogens. *Nature*, **160**, 892-895.

CASE, R. A. M., HOSKER, M. E., MCDONALD, O. B. and PEARSON, J. T. (1954). Tumours of the urinary bladder in workmen engaged in the manufacture and use of certain dyestuff intermediates in the British chemical industry. 1. The role of aniline, benzedine, alpha-naphthylamine and beta-naphthylamine. *British Journal of Industrial Medicine*, **11**, 75-104.

COLE, P., MANSON, R. R., HANING, H. and FRIEDELL, G. H. (1971). Smoking and cancer of the lower urinary tract. *New England Journal of Medicine*, **284**, 129-134.

EVANS, I. A. and OSMAN, M. A. (1974). Carcinogenicity of bracken and shikimic acid. *Nature*, **250**, 348-349.

LOCKWOOD, K. (1961). On the aetiology of bladder tumors in København-Frederiksberg: an inquiry of 369 patients and 369 controls. *Acta Pathologica et Microbiologica Scandinavica*, **51**, Suppl. 145, 1-66.

RADOMSKI, J. L., BRILL, E., DEICHMANN, W. B. and GLASS, E. M. (1971). Carcinogenicity testing of N-hydroxy and other oxidation and decomposition products of 1- and 2-naphthylamine. *Cancer Research*, **31**, 1461-1467.

ROSE, G. A. (1972). A simple and rapid method for the measurement of plasma ultrafiltrable and ionized calcium. *Clinica Chimica Acta*, **37**, 343-349.

ROSE, G. A. and WALLACE, D. M. (1973). Observations on urinary chemiluminescence of normal smokers and non-smokers and of patients with bladder cancer. *British Journal of Urology*, **45**, 520-533.

SCHLEGEL, J. U., PIPKIN, G. E., NISHIMURA, R. and DUKE, G. A. (1969*a*). Studies in the aetiology and prevention of bladder carcinoma. *Journal of Urology*, **101**, 317-324.

SCHLEGEL, J. U., PIPKIN, G. E. and SHULTZ, G. N. (1969*b*). The aetiology of bladder tumours. *British Journal of Urology*, **41**, 718-723.

STEELE, R. H. (1966). Aromatic carcinogenic hydrocarbons: possible role of electronic excitation states in carcinogenesis. *Bulletin of the Tulane University Medical Faculty*, **25**, 59-65.

WILLSTÄTTER, R. and KÜBLI, H. (1908). Reductions of nitro compounds by Zinin's method. *Chemische Berichte*, **41**, 1936-1940.

The Author

G. A. Rose, DM, FRCP, MRCPath, FRIC, Consultant Chemical Pathologist.

Correspondence to St Paul's Hospital, Endell St., London, W.C.2.

British Journal of Urology (1976), **48**, 72 ©

Short Case Report

Female Hypospadias

Hypospadias in the female is a very rare disorder (Funyu, Suzuki and Shirina, 1974). Aside from the 35 cases collected from the literature by Blum in 1904 and the additional 46 reviewed by Campbell and Harrison in 1970, only sporadic cases have been reported. This paper presents such a case which was successfully treated in our department.

Case Report

A 27-year-old woman, who was otherwise in good health, sought advice because of incontinence of urine. From infancy she had never been completely dry. She used to void urine frequently in an attempt to keep herself dry. From time to time she suffered from bouts of fever due to urinary tract infection. After she began having sexual intercourse at about the age of 20, she became completely incontinent.

On examination the patient was found to be in good general condition. The external genitalia were normal in appearance. The external urethral meatus was absent (Fig.). Vaginal examination revealed a wide open bladder neck freely communicating with the proximal part of the vagina. The rest of the physical examination showed no abnormality. Blood chemistry was within normal limits. The urine contained numerous leucocytes and culture revealed the presence of *B. coli*. Intravenous pyelography showed a normal upper urinary tract. The bladder was of normal size and contrast medium appeared in the vagina. An attempt to perform a cystography failed because of the wide communication between the bladder and vagina.

Operative Procedure

The urine was diverted by suprapubic cystostomy and a pubo-vesical fixation was performed in the hope that this might help in obtaining continence.

The urethral reconstruction was performed from a longitudinal strip of the anterior vaginal wall.

The postoperative course was uneventful. On follow-up examination she was completely continent. A urethral catheter passed freely through the urethra into the bladder. A cystourethrography showed a normal bladder and urethra with no leakage of contrast medium into the vagina.

Comment

The aetiology of congenital urethro-vaginal communications is a failure in the development of the vesico-urethro-vaginal septum. Blum (1904) divided them into 3 categories: 1. A deficiency of the posterior wall of the urethra and the anterior wall of the vagina, producing a longitudinal communication between the 2 organs; 2. Persistence of the urogenital sinus, with the vagina entering the urethra; 3. Vaginal urethra with the urethral meatus in the vagina proximal to the hymen.

Our case would seem to belong to Group 1 of this classification.

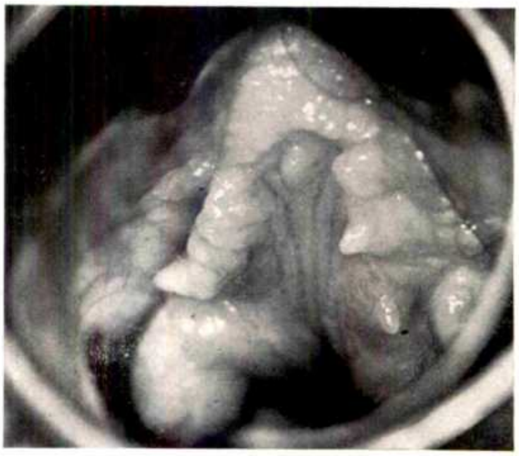
J. Fischelovitch and M. Ben-bassat,
Department of Urology and Department of Plastic Surgery, Beilinson Medical Center, Tel-Aviv Medical School, Petach-Tileva, Israel

References

Blum, U. (1904). Die Hypospadias der weiblichen Harnrohre. *Mber. Urol.*, **9**, 522-544.

Campbell, M. F. (1970). Hypospadias in the female. In *Urology*, ed. M. F. Campbell and J. H. Harrison, 3rd ed., vol. 2, Philadelphia: Saunders, pp. 1606-1607.

Funyu, T., Suzuki, T. and Shiraina, X. (1974). Female hypospadias: method of reconstructive surgery of the defective urethral wall. *Urologia Internationalis*, **29**, 114-122.



British Journal of Urology (1976), **48**, 73-75 ©

Preliminary Communication

The Effect of Bromocriptine in Patients with Benign Prostatic Hypertrophy

D. J. FARRAR and J. S. PRYOR
Departments of Urology and Medicine, Norfolk and Norwich Hospital, Norwich

The anterior pituitary hormone prolactin has been shown experimentally to have an effect on prostatic size. Its administration in a hypophysectomised rat results in an increase in prostatic weight (Grayhack and Libowitz, 1967) and when prolactin antiserum is administered to rabbits there is a marked reduction in prostatic size (Asano *et al.*, 1971). The synthesis of a specific central prolactin antagonist bromocriptine (2-bromo-α-ergocryptine: CB 154 Sandoz) prompted its use in a clinical trial in patients with signs and symptoms of benign prostatic hypertrophy to ascertain its effect on prostatic size *in vivo* and its possible clinical value.

Material and Methods

14 male patients aged 57-78 years (mean age 65 years) took part in a double blind, cross-over trial of bromocriptine and a placebo. Patients included in the trial were all on the routine waiting list awaiting prostatectomy and had had symptoms associated with benign prostatic hypertrophy for at least 2 years. Selection from the waiting list was at random, only patients with clinical evidence of prostatic carcinoma or those receiving medication which would affect the action of bromocriptine were excluded. The patients' informed consent to the trial was obtained.

The trial lasted for 16 weeks and patients were allocated into the trial in a random manner. 8 patients were treated initially with bromocriptine for 8 weeks, followed by an 8-week course of the placebo; the remaining 6 patients started with an 8-week course of the placebo followed by an 8-week course of bromocriptine. Each patient took 1 capsule twice daily, the active capsules each contained 2·5 mg of bromocriptine and identical capsules containing an inert powder constituted the placebo.

The patients' response to treatment was assessed on the basis of urinary symptoms and urine flow rates.

Urinary symptoms were assessed by a score system. Each of the symptoms of urgency, urge incontinence, hesitancy, terminal dribbling and dysuria, were allocated a number from 0-3 depending upon the severity of the symptoms (*e.g.* 0 = symptomless: 1 = mild disability: 2 = moderate disability: 3 = severe disability). The patient was also asked to assess the force of his urinary stream on this basis and similarly the frequency of diurnal and nocturnal voiding was enumerated. In this way a numerical value was obtained for the severity of each patient's symptoms at his initial visit. These symptoms were reassessed at each subsequent monthly visit during the trial; all patients being seen by the same observer (D. J. F.).

Urinary flow rates were measured using a Disa Mictiograph. The flow rate was measured on two occasions prior to the start of the trial and the faster flow recorded was taken as the baseline value. At each subsequent monthly visit a further flow rate was measured, care being taken to ensure that the minimum urinary volume voided was greater than 150 ml.

Prostatic size was estimated at rectal examination prior to treatment and at each monthly visit. The blood pressure, both erect and supine; haemoglobin, white cell count, erythrocyte sedimentation rate; serum electrolytes and urea, liver function tests and serum acid phosphatase were also measured and mid-stream urine specimens cultured.

All patients had a pre-treatment intravenous pyelogram and renogram. Those patients who completed the trial had a post-treatment renogram.

Results

9 of the 14 patients who entered the trial completed it.

Of the 5 patients who did not complete the trial, 1 had a hypotensive episode after the first dose of bromocriptine and withdrew from the trial, 3 patients developed nausea, lethargy, headache and unsteadiness whilst on the bromocriptine which resulted in their stopping treatment and 1 patient, who had marked unsteadiness even with the placebo, was excluded from the trial.

6 of the 9 patients who completed the trial obtained marked symptomatic relief on bromocriptine and 3 patients benefited from the placebo. Patients with troublesome frequency, nocturia, urgency or urge incontinence noticed much greater improvement in those symptoms following treatment with bromocriptine than with the placebo, although this improvement was not always attended by improvement in the flow rates. On the other hand, there was no significant difference in the improvement noticed in the symptoms of hesitancy, terminal dribbling and dysuria between the 2 treated groups and patients reported an equal improvement in the force of their urinary stream following treatment with both bromocriptine and the placebo, although there was little correlation between the patients' assessment of the force of their urinary stream and the measured peak urinary flow rate either initially or during treatment.

All patients at the initial assessment had peak urinary flow rates of less than 12·5 ml/sec on a minimum volume of 150 ml. Following treatment with bromocriptine there was marked improvement in the peak flow rates of 3 patients (6, 10 and 12·5 ml/sec to 15, 17 and 17·5 ml/sec respectively) but no improvement in the remaining 6 patients. Following treatment with the placebo there was neither improvement in the flow rates nor was the improvement obtained with bromocriptine maintained.

The blood urea and creatinine of all patients was normal throughout the trial. There was no change in the total blood counts or blood chemistry, with either bromocriptine or the placebo. All mid-stream urine specimens were sterile.

There was no change in prostatic size on rectal examination in either treatment group.

At the initial assessment 7 patients were found to be normotensive and 2 had diastolic blood pressures above 100 mm Hg. There was no significant change in blood pressure measured either erect or supine following treatment with bromocriptine or with the placebo in patients who completed the trial.

There was no significant abnormality on the intravenous pyelogram in any patients in the study; nor was there any significant change in the pre- and post-treatment renograms of patients completing the trial.

Nausea on first starting treatment with bromocriptine was noticed by 4 of the 9 patients who completed the trial. 2 patients had mild indigestion and 1 patient had mild postural hypotension but all these symptoms resolved during treatment.

4 of the 9 patients who completed the trial considered their symptoms to have improved sufficiently to warrant their removal from the waiting list for prostatectomy.

Interpretation of Results

Any trial of "pills for the prostate" is bedevilled by the lack of any readily accepted criteria for the assessment of the results of treatment. In this trial we have evaluated the patients' response objectively by the measurement of peak urinary flow rates and clinically by the study of micturition symptoms.

The measurement of peak urinary flow rates gives some indication of the degree of outflow obstruction, although it is important not to over-interpret them in the absence of pressure measurements, but marked changes occurring during treatment are probably significant. Peak urinary flow rates of less than 10 ml/sec are indicative of severe obstruction in the male (Claridge, 1966; Turner Warwick *et al.*, 1973) and all but 1 of the patients in this trial fell into this group. Whilst treatment with the placebo did not result in any improvement in flow rates, there was a significant improvement in 3 patients following treatment with bromocriptine and in 2 cases this was associated with an improvement in symptoms. This would suggest that there had been some reduction in the outflow resistance in these cases.

The overall improvement in micturition symptoms which occurred during the trial was not unexpected as the improvement of prostatic symptoms following the administration of a placebo is well documented (Castro, Griffiths and Edwards, 1971). However, the marked improvement in the symptoms of frequency, nocturia, urgency and urge incontinence with bromocriptine which did not occur with the placebo, was most striking. It has been shown (Turner Warwick *et al.*, 1973) in a series of patients with prostatic outflow tract obstruction that when these symptoms are present together, in the absence of urinary tract infection, they are commonly due to an underlying unstable bladder and that following the relief of the outflow tract obstruction by prostatectomy the bladder may return to a stable state with a subsequent relief of symptoms. It is probable that the patients in this series with frequency, nocturia, urgency or urge incontinence had underlying detrusor instability, but in only 1 patient of those who benefited from bromocriptine was there any objective evidence of decreased outflow tract obstruction with an improvement in flow rate; and it would seem unlikely that overall the relief of symptoms was due to relief of the outflow tract obstruction. Rather it would suggest that bromocriptine was acting to modify unstable detrusor activity, and support for this comes from a study of the action of this drug on detrusor instability in the absence of outflow tract obstruction (Farrar and Osborne, 1976).

The high incidence of side-effects in this series is directly attributable to an overdosage of bromocriptine, and these side-effects have recently been documented (Thorner, 1975). It is probably advisable when using bromocriptine in patients with benign prostatic hypertrophy to start at a lower dose then 2·5 mg b.d.

Whilst it is not possible to draw statistically significant conclusions from this trial because of the small number of patients completing the trial, the results suggest that bromocriptine does have an action, directly or indirectly on the lower urinary tract in man, possibly on both the prostate and bladder. A further evaluation of the therapeutic value of this drug on patients with benign prostatic hypertrophy is required.

Summary

A double blind trial of bromocriptine in the treatment of 14 patients with the symptoms of benign prostatic hypertrophy is reported.

5 patients did not complete the trial mainly because of side-effects due to an overdosage of bromocriptine.

In the remaining 9 patients there was symptomatic improvement in 6, with objective evidence of improvement in 3 patients on flow rate measurements.

The possible modes of action of bromocriptine in this condition are discussed.

We are grateful to Mr N. Alan Green and Mr M. Handley Ashken for permission to study patients under their care. We would like to thank Sandoz (Basle) for supplying the bromocriptine and also Miss C. A. Jones for her secretarial assistance.

References

Asano, M., Kanzaki, S., Sekiguchi, E. and Tasaka, T. (1971). Inhibition of prostatic growth in rabbits with antiovine prolactin serum. *Journal of Urology*, **106**, 248-252.

Castro, J. E., Griffiths, H. J. L. and Edwards, D. E. (1971). A double-blind, controlled, clinical trial of spironolactone for benign prostatic hypertrophy. *British Journal of Surgery*, **58**, 485-489.

Claridge, M. (1966). Analysis of obstructed micturition. *Annals of the Royal College of Surgeons*, **39**, 30-53.

Farrar, D. J. and Osborne, J. L. (1976). The use of bromocriptine in the treatment of the unstable bladder. *British Journal of Urology* (In press), **48**.

Grayhack, J. T. and Lebowitz, J. M. (1967). Effect of prolactin on citric acid of lateral lobe of prostate of Sprague-Dawley rat. *Investigative Urology*, **5**, 87-94.

Thorner, M. O. (1975). Dopamine is an important neurotransmitter in the autonomic nervous system. *Lancet*, **1**, 662-664.

Turner Warwick, R. T., Whiteside, C. G., Arnold, E. P., Bates, C. P., Worth, P. H. L., Milroy, E. G. J., Webster, J. R. and Weir, J. (1973). A urodynamic view of prostatic obstruction and the results of prostatectomy. *British Journal of Urology*, **45**, 631-645.

The Authors

D. J. Farrar, FRCS, Urological Registrar (now Senior Registrar, Department of Urology, Manchester Royal Infirmary).

J. S. Pryor, MRCP, Consultant Physician.

British Journal of Urology (1976), **48**, 76 ©

Short Case Report

Posterior Urethral Valves in Siblings

AMICUR FARKAS and DONALD G. SKINNER
Department of Surgery, Division of Urology, UCLA School of Medicine, Los Angeles, California 90024, *USA.*

Documentation of the familial occurrence of hypospadias, cryptorchidism, vesico-ureteric reflux and congenital uretero-pelvic junction obstruction has prompted the establishment by the American Academy of Pediatrics of a national registry of families in whom more than one sibling has a congenital genito-urinary anomaly. We recently treated 2 brothers with posterior urethral valves causing severe damage to their upper urinary tracts. To our knowledge, no similar anomaly has been reported among siblings in the English literature.

Case Report

A 7-day-old boy had urinary retention with overflow dribbling. Intravenous urogram and voiding cysto-urethrogram revealed a hydronephrotic right kidney, a non-functioning left kidney associated with posterior urethral valves, mega-ureters, and vesico-ureteric reflux (Fig. 1). He underwent fulguration of the valve, left nephro-ureterectomy and urinary reconstruction.

Aware of the disease in their youngest child, the parents brought in his older brother, age 2 years, for urological evaluation. He was reported to be without symptoms. Urinalysis, however, revealed pyuria and radiographic studies demonstrated disease that was identical, although mirror-imaged, to that of his brother. A non-functioning right kidney was demonstrated on IVP with massive hydronephrosis. A voiding cysto-urethrogram revealed posterior urethral valves with bilateral ureteral reflux and mega-ureters (Fig. 2). He also underwent fulguration of the posterior urethral valve, right nephro-ureterectomy, and subsequent urinary reconstruction.

Comment

Siblings of children with congenital genito-urinary anomalies should be scrutinised closely to detect similar anomalies before irreversible damage may occur. That the younger infant's anomaly triggered discovery of his brother's similar asymptomatic problem may have prevented further serious renal damage.

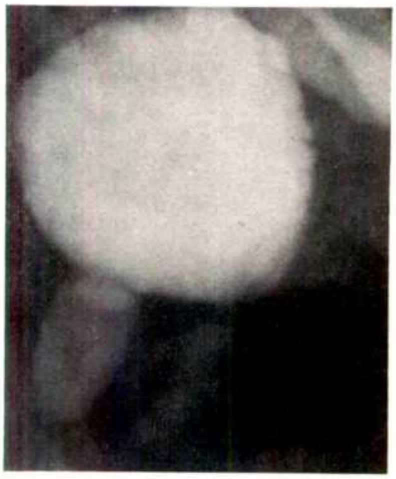


Fig. 1. Voiding cysto-urethrogram showing ureteric reflux and posterior urethral valves.

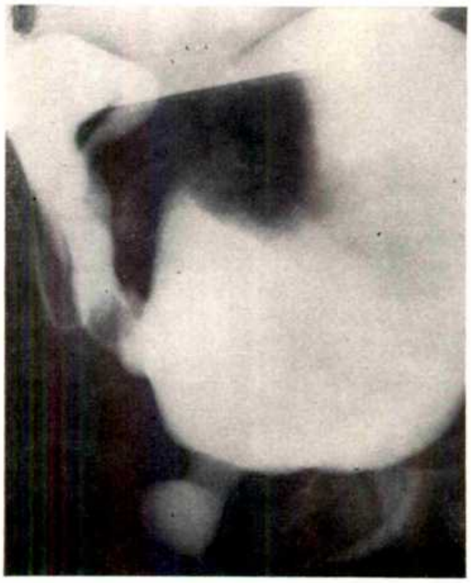


Fig. 2. Voiding cysto-urethrogram showing posterior urethral valves associated with ureteric reflux.

British Journal of Urology (1976), **48**, 77-81 ©

A Study of Concentrations of Trimethoprim-Sulphamethoxazole in the Human Prostate Gland

N. F. DABHOIWALA, A. BYE and M. CLARIDGE
Kent and Canterbury Hospital, Canterbury, Kent

Winningham, Nemoy and Stamey (1968) first drew attention to the requirements of an antibiotic effective in the cure of chronic bacterial infection of the prostate. It had to be mainly unionised at plasma pH because this form is relatively lipid soluble and favours diffusion. As prostatic fluid is acid relative to blood the antibiotic would thus become ionised and the ions trapped because their lipid solubility is low. The properties of trimethoprim (TMP) fit these requirements to some extent and Reeves and Ghilchik (1970) showed in dogs that a concentration gradient of TMP between plasma and prostatic fluid accorded with the hypothesis of ion trapping. However in man the actual pH of prostatic fluid is difficult to measure because of contamination with seminal vesicular fluid and in studies where TMP has been administered high urine concentrations of the drug may vitiate the prostatic fluid assay. This study sought to obviate these difficulties by direct assay of prostatic tissue obtained surgically and of plasma obtained simultaneously. As TMP was administered together with sulphamethoxazole (SMX), assays of this compound were also made.

Materials and Methods

The study was in 2 parts and contained 10 patients in each part. In the first, group (A), patients took a single loading dose of 4 co-trimoxazole tablets (320 mg TMP : 1,600 mg SMX) about 2-4 hours before surgery and in the second, group (B), they took the standard recommended therapeutic course (320 mg TMP : 1,600 mg SMX per day) for 1 week, the last dose being about 9 hours before surgery. The patients all underwent surgery at which prostate and plasma were sampled for assay of TMP and SMX.

Patient Selection

Patients were selected at the Department of Urology, Kent and Canterbury Hospital, from among informed volunteers. They all required a prostatectomy for obstructive symptoms and their renal function was near normal, as indicated by a blood urea level of 50 mg % or less. Those fit for an immediate elective prostatectomy were assigned to group A. Those requiring preoperative preparation and re-assessment were selected for the second group B. Some of the patients in both groups had indwelling catheters preoperatively.

Assay Methods

TMP—the spectrofluorimetric method of Schwartz, Koechlin and Weinfeld (1969) was used with modifications described by Fowle *et al.* (1975).
SMX—the semiautomated method of Bye and Fox (1974) was used.

Table I

The Levels of Trimethoprim (TMP) and Sulphamethoxazole (SMX) in the Prostate Gland with Simultaneous Levels in Plasma after a Single Dose of Co-Trimethoxazole (4 Tablets)

Patient (prostate sample)	Time after dose (hr)	TMP μg/g	"Active" SMX-BH μg/g	"Total" SMX-AH μg/g
1	3·5	9·8	13·3	26·5
2	2·8	3·6	9·7	16·4
3	3·0	3·4	11·9	14·8
4	3·5	3·4	13·5	23·5
5	3·0	1·7	1·2	3·9
6	3·8	1·4	<1·0	2·6
7	2·0	3·5	4·5	7·2
8	3·5	2·9	11·6	22·2
9	2·8	3·4	3·5	4·4
10	2·5	2·5	7·2	9·7
		mean 3·6	mean 7·6	mean 13·1

Patient (plasma sample)	Time after dose (hr)	TMP μg/ml	SMX-BH μg/ml	SMX-AH μg/ml
1	3·5	5·0	26·0	33·0
2	2·8	3·5	30·5	39·4
3	3·0	5·7	29·1	43·7
4	3·5	3·9	142·0	246·0
5	3·0	1·3	30·5	50·2
6	3·8	0·8	22·0	39·2
7	2·0	2·8	26·0	50·0
8	3·5	2·5	39·3	92·3
9	2·8	0·3	17·5	40·8
10	2·5	4·7	94·0	125·0
		mean 3·0	mean 45·7	mean 76·0
Ratio	$\frac{\text{Prostate}}{\text{Plasma}}$	1·17	0·16	0·13

Preparation of Specimens

From the prostatectomy specimen (transurethral or open) at least 2 g of tissue was immediately set apart. It was then thoroughly rinsed in McIlvaine's buffer solution, in an attempt to remove blood, blotted dry, bagged in plastic containers and stored in a deep freeze at below −10°C, together with the plasma, until collected for analysis. All tissues were thoroughly homogenised with 2 volumes of deionised water at 4°C before analysis. Pre-extraction of the tissues was needed for the SMX assays.

At the time of prostatectomy 10 ml of venous blood was collected in heparinised tubes. Immediately after surgery, this was centrifuged to separate the plasma. The latter was then labelled and stored in a deep freeze at below −10°C until collected for analysis.

Data Analysis

The plasma and prostate samples were sent for analysis to the Wellcome Research Laboratories, Beckenham, Kent in dry ice containers. The data in Tables I and II were analysed statistically by matched pairs "t" test.

Results

In group A (see Table I) the mean TMP level in plasma after dosing was 3·0 μg/ml and in the prostate 3·6 μg/ml. The difference was not significant $(P > 0{\cdot}20)$. For "biologically active" SMX the mean levels were 45·7 μg/ml

Table II

The Levels of TMP and SMX in the Prostate Gland with Simultaneous Plasma Levels after 2 Co-Trimoxazole tablets b.d. for 7 days

Patient (prostate sample)	Time after last dose (hr)	TMP μg/g	"Active" SMX-BH μg/g	"Total" SMX-AH μg/g
1	12·5	1·5	6·1	9·4
2	8·5	15·9	26·6	41·5
3	10·8	3·7	11·7	11·8
4	10·0	13·8	26·8	51·6
5	10·0	0·8	20·1	32·0
6	11·5	11·3	13·8	50·5
7	12·5	14·5	27·0	42·5
8	5·0	5·5	10·8	12·7
9	4·5	10·2	13·4	23·5
10	7·5	4·5	14·0	21·0
		mean 8·2	mean 17·0	mean 29·7

Patient (plasma sample)	Time after last dose (hr)	TMP μg/ml	SMX-BH μg/ml	SMX-AH μg/ml
1	12·5	0·9	15·0	24·0
2	8·5	6·2	53·0	91·0
3	10·8	2·9	43·0	77·0
4	10·0	6·0	63·0	120·5
5	10·0	3·8	78·0	114·0
6	11·5	4·5	55·0	109·5
7	12·5	4·5	70·0	112·0
8	5·0	3·1	28·0	46·2
9	4·5	5·5	39·0	52·0
10	7·5	3·1	43·0	70·8
		mean 4·0	mean 48·7	mean 81·7
Ratio	$\frac{\text{Prostate}}{\text{Plasma}}$	2·03	0·35	0·36

and 7·6 μg/ml respectively and significantly different ($P < 0{\cdot}01$). Likewise the "total" SMX level of 76·0 μg/ml and 13·1 μg/ml respectively were significantly different ($P < 0{\cdot}01$). The mean time between dosing and sampling was 3 hours with extremes of 2 and 3·7 hours.

In group B (see Table II) the mean TMP level in plasma was 4·0 μg/ml. This did not differ significantly from the levels seen in group A. The mean level of TMP in the prostate was 8·2 μg/ml which differed significantly ($P < 0{\cdot}01$) from the corresponding plasma level. For "biologically active" SMX the mean levels were 48·7 μg/ml in plasma and 17·0 μg/ml in prostate which differ significantly ($P < 0{\cdot}001$). Likewise the mean "total" SMX levels were 81·7 μg/ml and 29·7 μg/ml respectively which also differ significantly ($P < 0{\cdot}001$). The mean time between last dose and sampling was 9·3 hours with extremes of 4·5 and 12·5 hours.

Discussion

In a group of 24 commonly isolated urinary pathogens Bushby and Bushby (1975) reported the Minimum Inhibitory Concentration (M.I.C.) range for TMP between 0·6 and 2 μg/ml. For SMX 4 organisms were resistant and the remaining 20 had a M.I.C. range between 3 and 24 μg/ml. In every case except 5 synergy between TMP and SMX was demonstrated.

In the results reported by us, all cases had prostate tissue levels for TMP above 0·6 μg/g and only 4 had less than 2 μg/g.

Thus in 16 of the 20 cases therapeutically effective levels of TMP alone were obtained in prostate tissue and in each of the remaining 4 cases allowing for the synergistic action of the 2 drugs a dose level was obtained which would have been effective against all the pathogens tested by Bushby.

The differences between the 2 experiments indicate that equilibrium for both drugs cannot be established quickly if it is reached at all. Winningham *et al.* (1968) also observed a delay in equilibration not fully consistent with the ion trapping hypothesis. Slow diffusion from blood to tissue does not adequately explain the results.

The homogeneity of the prostate samples must be considered. The prostate could have been contaminated with blood and extracellular fluids with different concentrations of the drugs. The samples were of pathological tissue, in most cases benign hyperplasia, and as identification of tissue was difficult, capsule and bladder neck fragments might have been included. The first source of error is more considerable and was met by washing the tissue thoroughly. This might have withdrawn some of the drug by diffusion from the tissue. The nature of the washing fluid was probably not important. In fact a potassium free fluid was used as an early intention, later abandoned, was to estimate the volume of intracellular fluid in the specimen by potassium estimations. The concentration refers to the wet weight after the washing procedure had occurred.

The wide range of TMP and SMX levels obtained in our results may be due to several factors. Although renal function was normal in the majority, in a few cases it was impaired (blood urea up to 50 mg %). TMP being a base and SMX an acid the absorption and excretion kinetics would vary for each drug and especially with changes in urinary pH. Lastly, the wide variations in sampling times from the last dose of co-trimoxazole must cause considerable differences between subjects in the levels of TMP and SMX in both prostate and plasma.

The ion trapping hypothesis relies on a simple derivation of the Henderson-Hasselbalch equation together with the assumption that only free unionised drug can pass across the cell membrane. Hence for a basic drug, at equilibrium,

$$\frac{\text{concentration of drug inside cell}}{\text{concentration of drug outside cell}} = \frac{1+\text{antilog}_{10}(\text{pKa}-\text{pH inside cell})}{1+\text{antilog}_{10}(\text{pKa}-\text{pH outside cell}).}$$

If this is so then assuming a pKa for TMP of 7·3 and plasma protein binding of 44% as suggested by Salmon, Fowle and Bye (1975) and binding to intracellular protein of the same order, the intracellular pH of prostatic tissue would be about 6·9. However, several discrepancies arise. First, our single dose study appears to disagree with the hypothesis unless a delay term other than that explained by diffusion is introduced. Secondly the prostatic fluid pH is asserted to be 6·6 by Stamey, Meares and Winningham (1970) which differs from our calculated tissue pH of 6·9. Indirect calculation of a mean pH value for prostatic tissue by means of a drug with the mobility of TMP may be of greater relevance than direct estimation of the pH of prostatic secretion.

Tissue concentrations of SMX never exceeded the corresponding plasma levels which is expected as SMX has a pKa of 5·9 and is about 70% bound to plasma proteins.

Although the "pH-partition" hypothesis is valuable in predicting the *in vivo* behaviour of a drug it can only be accurate when the pKa, pharmacokinetics and protein binding of the drug are known and the pH of the tissue fluid is reliable (Fowle and Bye, 1971).

Neither this work nor the work of Stamey *et al.* (1970) adequately elucidates the reason for the time delay before equilibrium in prostatic tissues becomes established and further investigation into this question is required.

However the high levels of TMP obtained in prostatic tissue combined with the adequately synergistic levels of SMX after 1 week's treatment with co-trimoxazole at the standard dosage suggest that there are good theoretical reasons for expecting such medication to be effective against bacterial prostatitis.

Summary

The ability of trimethoprim (TMP) and sulphamethoxazole (SMX) components of co-trimoxazole to penetrate the human prostate gland was investigated.

After a single 4-tablet dose TMP was evenly distributed between prostate and plasma, whereas SMX was mainly associated with plasma. Following a week's therapy significant accumulation of TMP was seen in the prostate relative to plasma whereas SMX although still associated with plasma had increased drug levels in prostate compared with the single dose study.

It is concluded that co-trimoxazole produces effective antibacterial levels in the human prostate and has indications in the treatment of prostatitis.

We wish to record our thanks to the Wellcome Research Laboratories, Beckenham, Kent, for their kind co-operation and assistance in the analysis of all the data as well as for the supply of co-trimoxazole tablets.

References

Bushby, S. R. M. and Bushby, M. B. (1975). Trimethoprim/sulphamethoxazole synergy and prostatitis. Presented at IXth International Congress of Chemotherapy. London, July, 1975 (in press).

Bye, A. and Fox, A. F. J. (1974). Modification of an automated method for measurement of sulphamethoxazole and its major metabolite in biological fluids. *Clinical Chemistry*, **20**, 288-293.

Fowle, A. S. E. and Bye, A. (1971). Concentrations of trimethoprim and sulphamethoxazole in human prostatic fluid. In *Advances in Antimicrobial and Antineoplastic Chemotherapy*, vol. 1-2, Prague: Urban and Schwarzenberg, pp. 1289-1290.

Fowle, A. S. E., Bye, A., Hariri, F., Middlemiss, D. and Naficy, K. (1975). Dosage of co-trimoxazole in childhood. *European Journal of Clinical Pharmacology*, **8**, 217-222.

Reeves, D. S. and Ghilchik, M. (1970). Secretion of the antibacterial substance trimethoprim in the prostatic fluid of dogs. *British Journal of Urology*, **42**, 66-72.

Salmon, J. D., Fowle, A. S. E. and Bye, A. (1975). Concentrations of trimethoprim and sulphamethoxazole in aqueous humour and plasma from regimens of co-trimoxazole in man. *Journal of Antimicrobial Chemotherapy*, **1**, 205-211.

Schwartz, D. E., Koechlin, B. A. and Weinfeld, R. E. (1969). Spectrofluorimetric method for the determination of trimethoprim in body fluids. *Chemotherapy Supplement*, **14**, 22-29.

Stamey, T. A., Meares, E. M. and Winningham, D. G. (1970). Chronic bacterial prostatitis and the diffusion of drugs into prostatic fluid. *Journal of Urology*, **103**, 187-194.

Winningham, D. G., Nemoy, N. J. and Stamey, T. A. (1968). Diffusion of antibiotics from plasma into prostatic fluid. *Nature*, **219**, 139-143.

The Authors

N. F. Dabhoiwala, MS, FRCS, FCPS, Urological Registrar (now Chief Assistant, Department of Urology, University of Amsterdam and Academic Hospital).

A. Bye, PhD (Biochem), Research Biochemist, Department of Clinical Pharmacology, The Wellcome Research Laboratories, Langley Court, Beckenham, Kent.

M. Claridge, MCh, FRCS, Consultant Urologist.

Requests for reprints: M. Claridge, Kent and Canterbury Hospital, Canterbury, Kent.

British Journal of Urology (1976), **48**, 82 ©

Short Case Report

Accessory Vas Deferens: A Case Report

Anomalies of the vas deferens are very rare. A double vas deferens without duplication of the testis or epididymis was described by Blecher in 1931. Saunders found a solitary case of accessory vas during his extensive dissection career of 20 years. In this case, the vas left the epididymis as a single tube which distally branched into a double tube which opened into the ejaculatory duct. Mathé and Dunn (1948) reported a case of double vas deferens associated with a solitary kidney. In this case the accessory vas started as a blind tube in the neighbourhood of the liver and, lower down, it apparently joined the seminal vesicle. Wescott and Dykhuizen (1967) reported a case of an accessory vas due to polyorchism.

Case Report

From a collection of specimens of testes kept for an examination a right testis was picked up because it showed a very prominent appendix of the epididymis. The spermatic cord had been severed and it was not possible to know to which cadaver the specimen belonged. On palpating the spermatic cord two structures with a whip-cord like consistency were distinctly felt which raised the suspicion of the presence of 2 vasa. The spermatic cord was therefore thoroughly dissected and 2 vasa of different sizes were identified (Fig. 1). The larger one was the normal one and it was continuous with the tail of the epididymis. The smaller one emerged at the junction of the head and body of the epididymis. Histologically, it was confirmed that both were vasa. However, the smaller vas had a smaller lumen and a thinner muscle coat than the normal vas.

Comment

The presence of an accessory vas is often alleged to be a cause for failure of vasectomy. In the present case, which is a proven case of an accessory vas, it was possible to suspect its presence by a mere palpation of the spermatic cord. This case emphasises the need for a thorough palpation of the spermatic cord at the time of vasectomy.

References

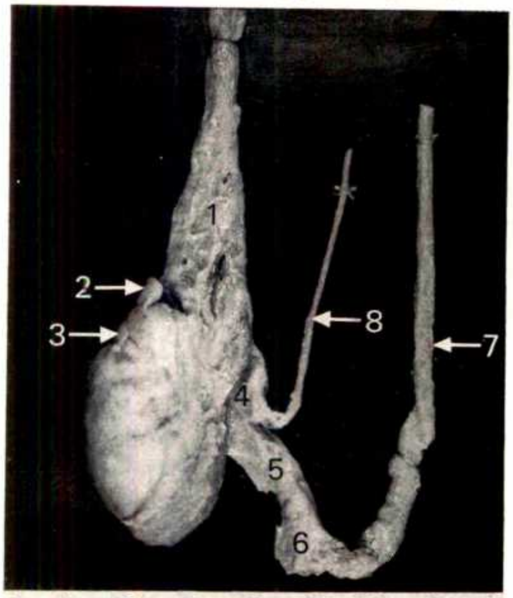
Blecher (1931). Über angeborene Missbildungen des Sämenleiters, insbesondere die einseitige isolierte Verdoppelung. *Deutsche Zeitschrift für Chirurgie*, **232**, 430-432. Quoted by **Mathé** and **Dunn** (1948).

Mathé, C. P. and **Dunn, G.** (1948). Double vas deferens associated with solitary kidney: case report. *Journal of Urology*, **59**, 461-465.

Saunders, J. B. de C. M. (1948). Personal communication. Quoted by **Mathé** and **Dunn** (1948).

Wescott, J. W. and **Dykhuizen, R. F.** (1967). Polyorchism. *Journal of Urology*, **98**, 497-500.

V. R. Mysorekar
Armed Forces Medical College, Poona-1, India.



Key.

1. Spermatic cord.
2. Appendix of epididymis.
3. Appendix of testis.
4. Head of epididymis.
5. Body of epididymis.
6. Tail of epididymis.
7. Vas deferens.
8. Accessory vas deferens.

British Journal of Urology (1976), **48**, 83-88 ©

Badenoch's Pull-through Operation for Urethral Stricture

G. H. TILAK, H. C. DHAYAGUDE and S. S. JOSHI
J.J. Hospital, Bombay, India

Techniques of urethral reconstruction as described by various authors (Solovov, 1935; Badenoch, 1950; Swinney, 1952; Johanson, 1953; Turner Warwick, 1960; Blandy, Singh and Tresidder, 1968) are available for the treatment of a urethral stricture partly depending upon its site. Strictures of the membranous and bulbomembranous urethra call for techniques described by Solovov (1935), Badenoch (1950) and Turner Warwick (1960).

This series presents 14 cases of stricture of membranous urethra, 12 cases treated by Badenoch's method, with a modification of the technique in 2 cases.

Material

From 1962 to 1974, 14 cases of stricture of the membranous urethra were treated at the J. J. Hospital, Bombay. The mean age of the patients was 32, the youngest being 13 years of age and the oldest 50 years of age.

Symptomatology

The symptoms most frequently encountered were dysuria and poor urinary stream. 9 patients presented with acute retention of urine and had to have a suprapubic cystostomy. (6 of these were referred to us after they had had an initial suprapubic cystostomy done elsewhere.) All these patients had a history of trauma to the perineum 5 patients having been involved in road traffic accidents. All these 5 patients had fracture of the ischio-pubic rami, 2 patients having slight disruption of the symphysis pubis.

It is interesting to note that 8 patients had a history of trauma to the perineum from 4 months to 15 years prior to the first appearance of symptoms of dysuria. Urinary incontinence was encountered in 3 patients, 1 of these having chronic retention with overflow incontinence; he was admitted in uraemia and was jaundiced. Impotence was encountered in all but 3 patients; one of them was only 13 years of age, the other 2 having had perineal trauma without any evidence of pelvic fracture or disruption of the symphysis pubis.

Diagnosis and Investigations

The diagnosis of stricture of the urethra is usually evident from a detailed history. The stream of micturition is observed and the investigations are then carried out. It is our routine, in all cases, to perform a retrograde urethrogram before instrumenting the urethra. The urethrogram is an excellent guide to define the site and extent of the stricture; and the state of the urethra proximal to the stricture.

Urine culture and sensitivity revealed almost 50% of cases with urinary infection, with the majority of the patients having *E. coli*, *Proteus vulgaris* and *Pseudomonas aeruginosa*, as the causative organisms.

An intravenous pyelogram and subsequently a micturating cystourethrogram are done to confirm the state of the renal function and the presence or absence of vesicoureteric reflux. The state of the bladder neck and the urethra proximal to the site of stricture can also be assessed. A cystogram and proximal urethrogram are done in cases having had an initial suprapubic cystostomy. The extent of the stricture and its site is a guide in selecting the procedure; whether a formal Badenoch's operation or its modification (*vide infra*).

Technique of Operative Procedure

Our preference is for a 2-stage procedure. If the patient has an associated bladder neck obstruction, this is resected through a suprapubic approach via a midline subumbilical incision and the bladder

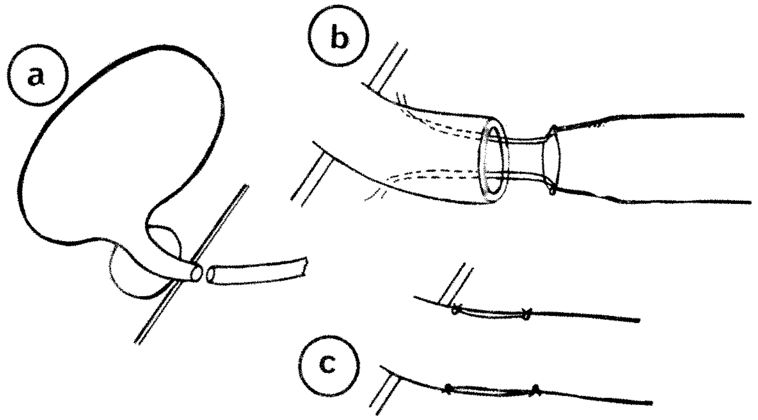


Fig. 1. Modified Badenoch's procedure. (a) Urethra cut across at, or just distal to, the perineal membrane; (b) urethra partially telescoped; (c) urethral ends fixed with catgut.

is closed leaving a Malecot catheter, as high in the suprapubic wound as possible. The staged procedure reduces the operating time at the second stage and also facilitates insertion of a catheter which acts as a splint at the pull-through operation.

The second stage is undertaken about 3 weeks after the first operation (by which time the suprapubic incision has healed completely). Both the stages are done preferably under spinal anaesthesia, with long-acting anaesthetic agent, *e.g.*, Nupercaine. We have not come across any untoward side-effects after such an anaesthetic agent. On the contrary, this type of anaesthesia gives full relaxation and provides a relatively bloodless field, which is certainly an added advantage.

The approach to the bulbomembranous urethra is through an inverted V incision (Blandy *et al.*, 1968) as against the original vertical incision employed by Badenoch (1950). It prevents soiling of the incision by faecal matter, which may occur if the posterior limit of the vertical incision is carried too far. It also gives a better exposure for the posterior urethra, which enables one to excise the periurethral scarred tissue. This step is essential for a successful reconstruction. We always mobilise at least 4-5 cm of the urethra distally. The stricture site is identified by passing a urethral bougie. The urethra is divided just distal to the stricture. Periurethral scarring over the membranous urethra is excised as much as possible. A Hey Grove's curved bougie is projected into the proximal urethra through a suprapubic route, and the midline incision is made over the tip of the bougie. If it is found that the opening is small, then the incisions are made in 3 and 9 o'clock positions, so that the incision will appear to be cruciate. The edges of the incision are trimmed, after which a 12/15 (approx 21/25 Fr.) Lister's bougie can easily be passed from below. The excess of spongy tissue of the distal urethra is excised so as to get the urethra in the shape of a pencil for facilitating the procedure of telescoping the urethra.

In cases where disruption of the puboprostatic ligament has occurred at the original injury (usually with pelvic fracture), a formal Badenoch's pull-through operation is undertaken. A Portex Nelaton's catheter size 21Fr. is used to act as a splint. This catheter is passed through the suprapubic opening and is brought into the perineal wound. The catheter is then passed into the distal urethra, which has already been "tailored". The distal urethra is then anchored to the catheter by a 4(0) chromic catgut stitch. This stitch passes through the wall of the urethra and the wall of the catheter. The ends of this catgut stitch are left long enough to encircle the catheter over the urethra where a firm knot is tied. The catheter and with it the urethra is pulled up till the distal urethra telescopes into the proximal urethra. Optimum tension is maintained to prevent

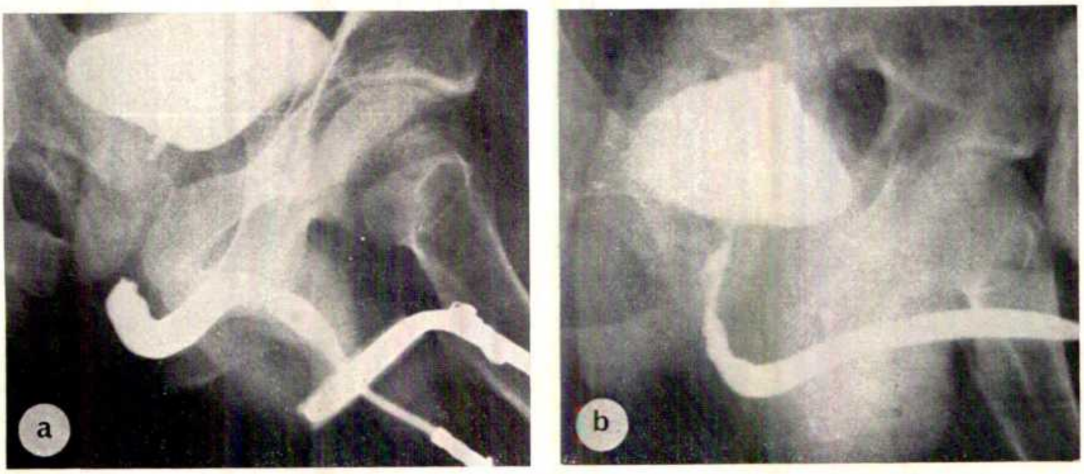


Fig. 2. (a) Preoperative urethrogram with membranous urethral stricuture; (b) Postoperative urethrogram after classical Badenoch's operation.

the urethra slipping out of position by applying a strong haemostat flush with the abdominal wall. The periurethral tissue is then approximated with 4(0) chromic catgut interrupted sutures. The bladder is drained with a Malecot's catheter which lies by the side of the catheter splint. The inverted "V" incision is closed in layers after leaving two corrugated drains, one over the periurethral area, the other subcutaneously. The drains are left in for 48 to 72 hours.

A modified Badenoch's procedure was done in patients with strictures up to 1 cm long just distal to the perineal membrane without much periurethral scarring. In these 2, the distal urethra was partially telescoped into the dilated proximal urethra. This is facilitated by means of 4 interrupted 4(0) chromic catgut sutures on an atraumatic needle. The sutures are taken at the 3, 6, 9 and 12 o'clock positions and tied firmly once all the stitches are taken. Further reinforcing stitches are then taken to take the tension off the initial sutures. These stitches are taken at the 3, 6 and 9 o'clock positions, picking up the periurethral tissue proximally and periurethral with minimal spongy tissue distally (Fig. 1). When all the sutures are in position, a Foley catheter (F 18 or F 16 gauge) is passed per urethram. A small size catheter is preferred to allow the urethral discharge to find its way out around the catheter. Such an indwelling catheter is left in the bladder for about 3 weeks, during which time the suprapubic catheter can easily be dispensed with.

Early Postoperative Follow-up

The splint is removed on the 14th day and a Foley catheter is passed per urethram by ordinary or by a railroad method. The suprapubic Malecot catheter is then removed. The urethral catheter is removed after the suprapubic fistulous opening and the wound have completely healed. A retrograde urethrogram is done the day the catheter is removed (Figs. 2b and 3b). Calibration is performed (usually under local anaesthesia) and repeated at about monthly intervals, until the stream is satisfactory and stable; this has usually been between 4 and 6 months.

Complications

1. **Wound Infection.** Three patients had local wound infection in the suprapubic region. These cases initially had urinary infection. Incidentally, 2 of these initially received treatment at other centres. The wound infection, however, was easily controlled with antibiotics.

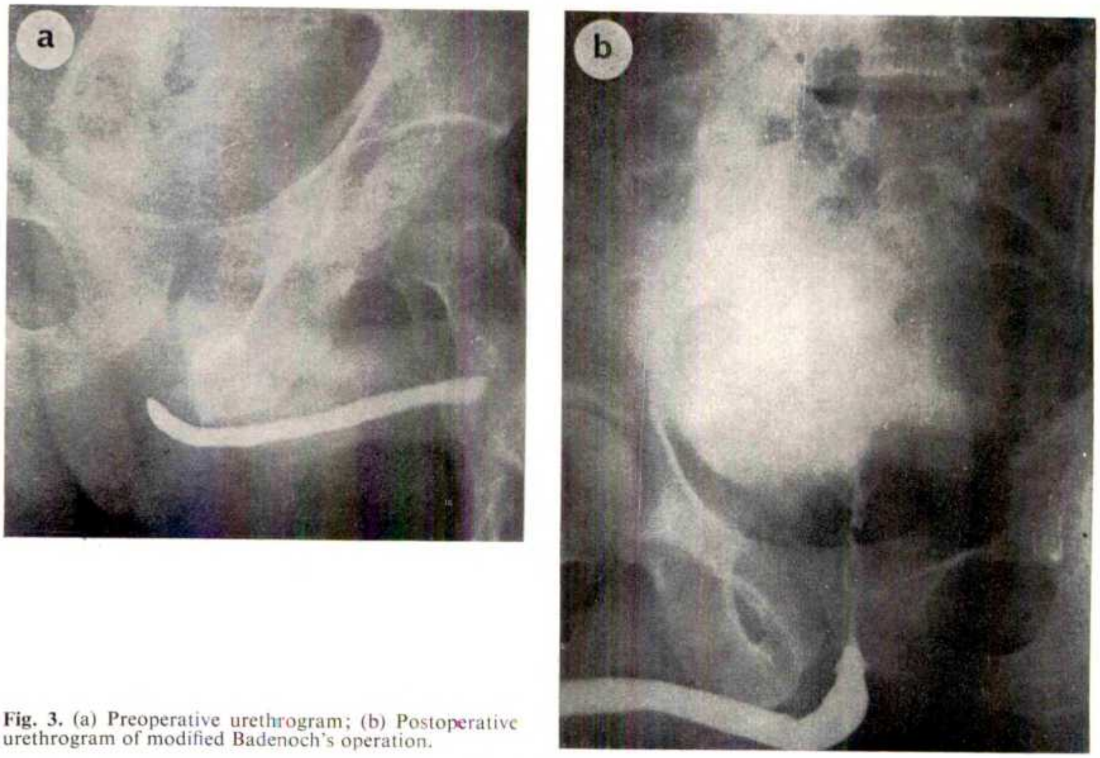


Fig. 3. (a) Preoperative urethrogram; (b) Postoperative urethrogram of modified Badenoch's operation.

2. **Haematoma and Gaping of the Perineal Wound.** One case developed a perineal haematoma. The wound gaped and had to be resutured and later skingrafting had to be done. Fortunately, the bulbospongiosus muscle apposition prevented the urethra from being exposed.

3. **Perineal Leak.** One patient had a perineal urinary leak, probably from the site of repair as revealed by the urethrogram (Fig. 4). The leak lasted for about 2 weeks and then stopped completely.

4. **Secondary Haemorrhage.** Mild secondary haemorrhage was encountered in 1 patient on the 8th postoperative day. This lasted for about 24 hours and was easily controlled by continuous irrigation through a suprapubic catheter.

5. **Restricture with Periurethral Abscesses.** One patient had an impassable stricture at the site of reconstruction, with periurethral abscesses. He had undergone a formal pull-through procedure 2 years prior to the development of the stricture. He, however, had failed to report for regular postoperative follow-up.

Results

14 patients have been treated for stricture of the membranous urethra over a period of 13 years. At the follow-up, urine culture, blood urea and if necessary a retrograde urethrogram are done.

This series shows that 10 of the 14 patients had a good result, 2 of these having undergone the modified procedure. Their stream is excellent, as is the urinary control. They do not require urethral dilatations and have a normal blood urea with no urinary infection. These patients had their operations from 6 months to 13 years ago.

Fair results were obtained in 3 patients where intermittent dilatation at an interval of 1 to 2 months is necessary. One of these has granulations at the site of repair (Fig. 5) and is being

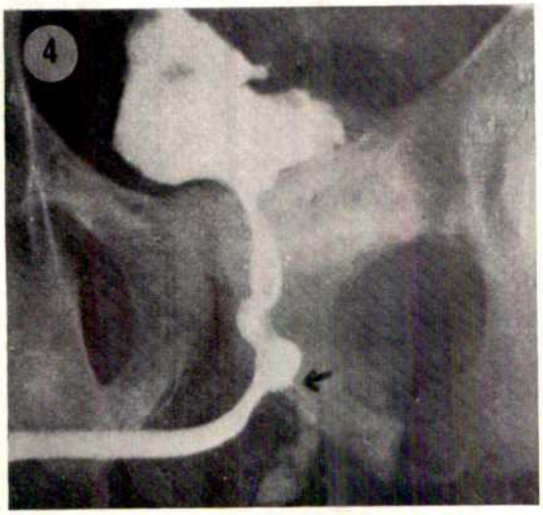


Fig. 4. Classical Badenoch's with postoperative urinary fistula.

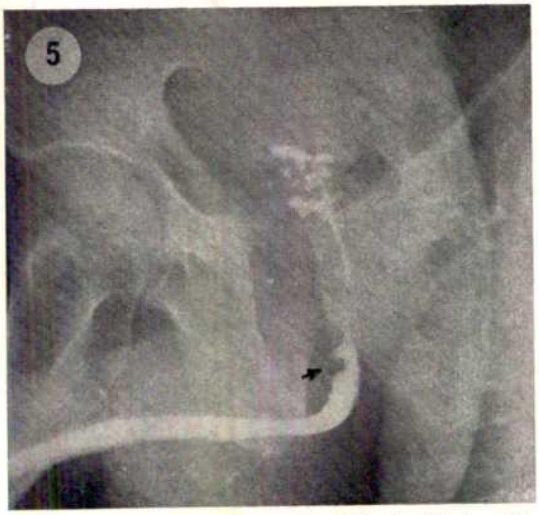


Fig. 5. Postoperative urethrogram of classical Badenoch's operation with granulation tissue.

considered for endoscopic fulguration. Nevertheless, they still have a satisfactory urinary stream.

The operation was a failure in 1 patient whose urethra has stenosed completely at the site of reconstruction, with periurethral abscesses. This occurred 2 years after the initial procedure. At present he has a suprapubic cystostomy; the periurethral abscesses have subsided. A Turner Warwick procedure is being considered to tackle the stricture.

Discussion

Strictures of the membranous urethra pose special problems owing to their inaccessible site for ordinary procedures. Badenoch's (1950), Turner Warwick's (1960) and Waterhouse's (1974) procedures have all been tried. Of these the first 2 have stood the test of time. The Badenoch's

Table I

Incidence of Stricture of Membranous Urethra, as Related to Fractured Pelvis

Stricture of membranous urethra	No. of patients
Patients with fracture of ischio-pubic rami	5
Patients without fracture of ischio-pubic rami	9

Table II

Stricture of the Membranous Urethra and its Association with Bladder Neck Obstruction

Stricture of membranous urethra	No. of patients
Cases with B.N.O.	5
Cases without B.N.O.	9

Table III

Type of Procedure employed in 14 Cases

Type of procedure	No. of patients
"Formal" Badenoch's pull-through operation	12
"Modified" Badenoch's procedure	2

Table IV

Follow-up in Years and Number of Patients

Years	No. of patients
Up to 1 year	2
1 to 3 years	3
3 to 6 years	4
6 to 10 years	3
10 to 13 years	2
Total	14

Table V

Results in Patients Treated for Membranous Urethral Stricture

Results	No. of patients
Good	10
Fair	3
Failure	1
Total	14

procedure and its modification, however, can be done as a one-stage procedure, which is advantageous to patients who object to repeated or multi-staged procedures. The morbidity by using a skin flap for urethral reconstruction can be completely eliminated. It has been observed (G. H. T.) in the past 15 years that in the East patients have profuse sweating and burning sensations in the perineal urethra in the hot and humid weather, when a skin flap is used for urethral reconstruction. In addition, formation of hypertrophic scar and growth of hair in the urethra cannot be completely eliminated. Last but not least is the feasibility of the Badenoch's and its modified procedure which can be done at centres where special equipment for reconstructive urethral surgery is not available.

Summary

14 patients with strictures in the region of the membranous urethra were treated by Badenoch's urethral pull-through operation or a slight modification of this.

The results were good in 10 of the cases.

This procedure has advantages over those using scrotal flaps in hot climates.

References

Badenoch, A. W. (1950). A pull-through operation for impassable traumatic stricture of the urethra. *British Journal of Urology*, **22**, 404-409.

—— (1956). Discussion on urethral injuries. *Proceedings of the Royal Society of Medicine*, **49**, 685-695.

—— (1968). Traumatic stricture of the urethra. *British Journal of Urology*, **40**, 671-676.

Blandy, J. P., Singh, M. and Tresidder, G. C. (1968). Urethroplasty by scrotal flap for long urethral strictures. *British Journal of Urology*, **40**, 261-267.

Johanson, B. (1953). In *Modern Trends in Urology*, ed. E. Riches, London: Butterworths, pp. 344-351.

Leadbetter, G. W. (1960). A simplified urethroplasty for strictures of the bulbous urethra. *Journal of Urology*, **83**, 54-59.

Solovov, P. D. (1935). Fracture of pelvis with injury of bladder and ureter. *Vestnik Khirurgii*, **37**, 36-48.

Swinney, J. (1952). Reconstruction of the urethra in the male. *British Journal of Urology*, **24**, 229-235.

—— (1957). Urethroplasty: an assessment after seven years' experiences. *British Journal of Urology*, **29**, 293-297.

Turner Warwick, R. T. (1960). A technique for posterior urethroplasty. *Journal of Urology*, **83**, 416-419.

—— (1968). The repair of urethral strictures in the region of the membranous urethra. *Journal of Urology*, **100**, 303-314.

Waterhouse, K., Abrahams, J. I., Caponegro, P., Hackett, R. E., Patil, U. B. and Peng, B. K. (1974). The transpubic repair of membranous urethral strictures. *Journal of Urology*, **111**, 188-190.

The Authors

G. H. Tilak, MS, FRCSE, Honorary Urologist.
H. C. Dhayagude, MS, FRCS, FRCSE, Pool Officer in Urology.
S. S. Joshi, MS, FRCS, Pool Officer in Urology (now Surgeon, Jaslok Hospital, Bombay).

Book Reviews

Cornell Seminars on Nephrology. Edited by E. LOVELL BECKER. (Perspectives in Nephrology and Hypertension, vol. 2.) Pp. 260 with 106 illustrations. Wiley, 1973. £10·60.

This book is the second volume of "Perspectives in Nephrology and Hypertension" and consists of a series of seminars given at the New York Hospital, Cornell Medical Center. The first chapter on chronic renal insufficiency is by Dr E. Lovell Becker who also edits the whole volume.

These up-to-date review articles will be of considerable help to specialists in general medicine as well as to many nephrologists.

Focal glomerular sclerosis by Churg and Grishman, recent knowledge about vitamin D metabolism and vitamin D analogues by DeLuca, glomerulonephritis in adults by Earle, neonatal renal physiology by Edelman—these are clear and authoritative as might be expected. The value of mixed immunosuppressive regimes based on laboratory experiments in animals presented by Friedman may have lessons applicable to human renal disease but controlled clinical trials are still generally lacking.

There is a nice chapter on the histology of acute renal failure by Heptinstall followed by one on pathogenetic mechanisms in acute post-streptococcal glomerulonephritis by Lange. A résumé of hypertension by Laragh includes his well-known theories on the role of renin. Renovascular hypertension is dealt with later by Vertes with a consideration of the part played by surgery. Micropuncture studies in the rat described by Oken, give further support to the notion that heavy proteinuria must be due primarily to increased glomerular permeability. There is also an intriguing account by Rennie of some of the changes which occur in renal function at high altitudes. Some immunological aspects of glomerulonephritis are discussed by McCluskey while West and others contribute a section on the nephritides associated with hypocomplementemia. Finally the controversy as to whether idiopathic hypercalciuria is primarily a gastro-intestinal or renal abnormality is discussed by Suki *et al.* They present fairly convincing evidence based on patients they have studied which suggests that the renal abnormality is more likely.

Containing as it does the condensed opinions, on an important and timely choice of topics, of a strong team of world authorities, this is altogether a pleasant and highly readable little book.

P. R. U.

Diagnostic and Therapeutic Aids in Urology. By HENRY BODNER. Pp. 332 with 76 illustrations and 5 tables. Springfield, Illinois: Charles C. Thomas, 1974. £12·38.

This book is billed on the cover as providing a comprehensive survey of "tricks of the trade" which do not appear in standard urology textbooks. Written by a senior and much respected Californian urologist who since 1957 has published a regular edition of the weekly urological clinical letter, the concept is full of promise.

In practice I found it rather disappointing. Investigations are described without reference to normal values or usefulness in clinical practice (measurement of the bladder neck diameter with a Kollman dilator is one such example) and other techniques are described in such a way as to make it clear that the author has had little, if any, experience of their use in practice. Many techniques are described in inadequate detail to be put into practice and references to the original articles describing these techniques would be a valuable addition to this book.

The book is aimed at American urologists and chapters on setting up of a urological practice have little relevance to the practice of urology in Britain, and the vasectomy consent form which apparently exonerates the surgeon from any responsibility at all for his surgical practice would certainly not stand up to legal scrutiny in this country. There are a number of tables, some useful (such as a list of those drugs implicated in urinary tract symptoms), others of virtually no use (such as flow rate down standard catheters of different makes).

Having said all this, however, many of the tips described in this book are worthwhile and there can be few urologists, however experienced, who will not gain a number of worthwhile points from a perusal of its well produced text. It is a book for the hospital or departmental library rather than one to keep on one's personal bookshelf.

J. C. S.

Dialysis, Transplantation, Nephrology. Edited by J. F. MOORHEAD (Proceedings of the European Dialysis and Transplant Association, vol. 11.) Pp. 582. Tunbridge Wells: Pitman, 1975. £13·50.

This book is the Proceedings of the meeting of the European Dialysis and Transplant Association held in Tel Aviv in 1974. It suffers from the problem that afflicts most similar publications in that by the time that it is published there has already been or is about to be another conference which relegates some of its contents to the realms of history. Thus the 1974 Statistical Report is superseded by the 1975 model actually distributed at the Copenhagen Conference. However many of the contributions are of lasting interest and value. I would put the contribution of Dr Habib on the classification of glomerulopathies in this category although the complete absence of photomicrographs renders even this work of little value to the non-nephrologist unfamiliar with renal histology. Probably the most important advance in dialysis in recent years has been the appreciation that dialysis times can be reduced to more socially acceptable levels by the use of large surface area dialysers. Biochemical evidence relating "middle molecules" (of molecular weight 1,300-1,500) to uraemic toxicity is reported (Man *et al.*) giving a rationale for the use of the large area dialysers. A mathematical approach to the individualisation of dialysis times is presented (Widerøe *et al.*) and has great appeal. Despite the report from the Editors group that hypertension can always be controlled by dialysis, the more general experience of the finding of a small group of resistant hypertensives requiring drug therapy or nephrectomy is again reported with the results of drug treatment.

There have unfortunately been no major advances in the field of transplantation but a number of refinements of management are reported. In summary the book is an essential acquisition for the library of any unit involved in dialysis but because of its emphasis on technique is probably of little interest to physicians and surgeons not intimately involved in the treatment of end-stage renal disease.

R. W.

Book Received

Hemodialysis in the Home. By G. Bazzato and G. Onesti. Springfield: Thomas, 1975. £4·30.

Announcement

European Association of Urology

Prize Essay Contest

The European Association of Urology has instituted two prize essay contests, one for clinical and the other for laboratory research in urology. Each award shall be of S.Fr. 2,000.

The winners will have a special place on the programme to read their paper during the 1976 Congress of the E.A.U. which is to be held in Prague from 24 to 26 September 1976.

Entries are limited to European doctors under the age of 35 years. The essay may represent individual work but if done by a group, the contestant must be the principal investigator.

The manuscript shall be in English and in proper form for publication in the official Journal of the Association: *European Urology*.

The prize essays will be published. Publication of any other essay in the Journal is subject to the decision of the Editorial Board. Essays with curriculum vitae of the author should be sent before 15 June, 1976, to the Secretary of the European Association of Urology, Prof. W. Gregoir, Department of Urology, Brugmann University Hospital, B-1020 Brussels, Belgium.

STIFTUNG C. E. ALKEN PRIZE

1. We would like to announce the establishment of an endowment fund under the name of Stiftung C. E. Alken, for the purpose of furthering clinical work and research in the field of Urology by presenting an annual award of SwF5,000 for outstanding scientific endeavours.
2. The award will be for an unpublished work in the field of Urology. It will be conferred prior to the annual Congress of the German Society for Urology and an award certificate will also be presented. The prize money may be divided among several contributors.
3. The papers may be written in either German or English and three copies have to be submitted by 1st March 1977, to:

Stiftungsrat C. E. Alken-Stiftung
Advokaturburo Dr E. Kellerhals
Bundesplatz 4
CH-3011 Bern
Switzerland.

4. Each submission must be affixed with a code word and must *not* bear the author's name. But, in addition, a sealed envelope labelled with the code word is to be included, containing on a separate sheet of paper the author's name and professional standing, together with the code word.
5. Upon the receipt of the submitted paper, the Endowment Fund acquires the option to publish it. This option is entirely independent of the actual award of the prize money. The judges will be required to announce their decision to take up this option within a period of four months after the submission deadline. If by this date no such announcement has been made, the publication rights will automatically revert to the author and his paper will be returned to him.
6. The adjudicators for the award will be the Board of Directors of the Endowment Fund and their decision will be final.

ERRATA

In the Short Case Report on *Unilateral Multicystic Kidney and Contralateral Hydronephrosis in the Newborn* on page 176 of the April 1975 issue, the first sentence in the 'Comment' should read—A 12-day-old girl and NOT a 12-year-old girl.

In the Short Case Report on *Intraperitoneal Rupture of Pyonephrosis* on page 488 in the October 1975 issue, the Figure was reproduced upside down.

In the Short Case Report on *Reversible Lymphomatous Non-Obstructive Uropathy* on page 524 in the October 1975 issue, the first sentence in the 'Comment' should read—Although renal involvement in the lymphoma is common, uraemia is usually caused by bilateral ureteric obstruction and is NOT due to renal parenchymal involvement alone.

Printed in Great Britain by T. & A. Constable Ltd., Hopetoun Street, Edinburgh

CURRENT UROLOGICAL LITERATURE: SELECT BIBLIOGRAPHY[1]

The list of Current Urological Literature is now arranged to correspond to the order in which papers are published in the *Journal*, *i.e.* in anatomical order beginning with papers on the kidney.

A general section is included at the end.

KIDNEY

General. Hematuria. (T. M. Goodman.) *Rhode Island Med. J.* 1975, **58**, 156.

Proteinuria in patients with uroepithelial tumours with special regard to tumour size, clinical staging and grade of malignancy. (B. Johansson and S. Kistner.) *Scand. J. Urol. Nephrol.* 1975, **9**, 45.

Congenital Anomalies. Development of the upper urinary tract in myelomeningocele and consequent urological care. (H. Madersbacher.) *Int. Urol. Nephrol.* 1975, **7**, 13.

Silent anomalies of urinary tract and congenital heart disease. (S. Rao *et al.*) *Chest*, 1975, **67**, 685.

Urinary and genital malformations associated in the female, surgical reimplantation of the ectopic found in the pelvis kidney. (E. Vincent.) *J. Urol. Néphrol.* 1975, **81**, 232.

Intrathoracic ectopic kidney. (R. G. Serrate *et al.*) *Med. Clin.* 1975, **64**, 21.

Crossed renal ectopia without fusion associated with carcinoma of urinary bladder. (V. S. Tiwari *et al.*) *Clinician*, 1974, **38**, 513.

Segmental hypoplasia of kidney. (H. P. Weber *et al.*) *Klin. Pädiat.* 1975, **187**, 264.

Abdominal aneurysm and horseshoe kidney: a review. (D. S. Bietz and K. A. Meredino.) *Ann. Surg.* 1975, **181**, 333.

Concomitant aortic aneurysm and horseshoe kidney. (W. R. McGregor *et al.*) *Rocky Mountain Med. J.* 1975, **72**, 205.

Horseshoe kidneys: 40-year experience. (W. R. Pitts and E. C. Muecke.) *J. Urol.* 1975, **113**, 743.

Some aspects in the radiological assessment of renal and ureteral duplication. (B. Ameratunga.) *Aust. Radiol.* 1975, **19**, 52.

Congenital urinary tract malformations: epidemiologic and genetic aspects. (E. Bois *et al.*) *Clin. Genet.* 1975, **8**, 37.

Trauma. Les contusions du rein. (P. Boggio and R. Ott.) *Helv. Chir. Acta*, 1975, **42**, 69.

Arteriography in the assessment of renal trauma. (E. K. Lang.) *J. Trauma*, 1975, **15**, 553.

Hypertension due to renal trauma. (M. Camey and A. le Duc.) *J. Urol. Néphrol.* 1975, **81**, 470.

Renal injury from blunt trauma in childhood. Radiological evaluation and review. (L. W. Young *et al.*) *Ann. Radiol.* 1975, **18**, 359.

Management of renal trauma in the child. (J. V. Raust *et al.*) *J. Radiol. Electr.* 1975, **56**, 533.

Recent advances in diagnosis and management of blunt renal trauma. (A. T. K. Cockett *et al.*) *J. Urol.* 1975, **113**, 750.

Traumatic veno-caliceal fistula in solitary kidney. (T. Tencer and L. Ross.) *J. Urol.* 1975, **113**, 856.

Spontaneous rupture of kidney secondary to polyarteritis nodosa. (P. E. Tocci *et al.*) *J. Urol.* 1975, **113**, 860.

Scintigraphical examinations in kidney trauma. (H. Kracht *et al.*) *Int. Urol. Nephrol.* 1975, **7**, 23.

Renal blood flow and function in the rabbit after surgical trauma. 1. An experimental study. 2. The role of construction in the main renal artery and activation of the alpha-adrenergic receptors. 3. Effects of temporary occlusion of renal artery. 4. Effects of ureteral ligation. (F. Lyrdal and T. Olin.) *Scand. J. Urol. Nephrol.* 1975, **9**, **129**, **142**, **151**, **161**.

Traumatic rupture of the kidney, conservative operation. (J. Ducassou *et al.*) *J. Urol. Néphrol.* 1975, **81**, 255.

Renal injuries. (T. S. Morse.) *Pediat. Clin N. Amer.* 1975, **22**, 379.

Acute renal failure in combat injuries. (A. Iaina *et al.*) *J. Trauma*, 1975, **15**, 281.

Effect of surgical trauma on the renal function. (V. V. Abbakumov.) *Ther. Arch.* 1975, **46**, 137.

Atraumatic rupture of the kidney. (S. Tønjum *et al.*) *Brit. J. Urol.* 1975, **47**, 145.

Disruption of the renal pelvis by blunt trauma. (T. B. Hopkins and L. A. Klein.) *J. Trauma*, 1975, **15**, 250.

A study of 137 cases of renal trauma. (J. P. Pryor and J. P. Williams.) *Brit. J. Urol.* 1975, **47**, 45.

Salt and water disturbance after serious injury in solitary kidney. (J. Bodeker and R. Nagel.) *Urologe*, 1975, **14**, 94.

Fistula. Renal arteriovenous fistula due to neoplasm. (J. M. Colas *et al.*) *J. Urol. Néphrol.* 1975, **81**, 423.

Spontaneous pyeloduodenal and renocolic fistulas. (J. E. Greene *et al.*) *Southern Med. J.* 1975, **68**, 641.

Traumatic arteriovenous fistula of the kidney: an unusual cause of hypertensive encephalopathy. (J. R. Kirkpatrick.) *J. Trauma*, 1975, **15**, 363.

Radiologic seminar CL: spontaneous closure of a renal arteriovenous fistula. (J. Trapp *et al.*) *J. Mississippi Med. Ass.* 1975, **16**, 91.

Infections. Detection of bacteriuria by dip-slide. Routine use in a large general hospital. (P. D. Ellner and T. Papachristos.) *Amer. J. Clin. Path.* 1975, **63**, 516.

The treatment of tuberculous stenosis of the renal pelvis by pyelo-ureteral plasty. (J. Ducassou and P. Cezilly.) *J. Urol. Néphrol.* 1975, **81**, 132.

Evaluation of the uriculture strip technic for systematic detection of kidney infections. (G. Pacaud and F. J. Chicou.) *Méd. Mal. Infect.* 1975, **5**, 174.

Use of the nitroblue tetrazolium (NBT) test in the differentiation between pyelonephritis and cystitis. (B. Björkstén and P. de Chateau.) *Acta Paediat. Scand.* 1975, **64**, 182.

Pyelonephritis—bane of upper tract. *Patient Care*, 1975, **9**, 44.

Über die Abhängigkeit des radionephrographischen Kurvenverlaufes von dem Hydratationszustand bei

---

[1] Titles in this list have been taken from those listed in *Current Contents: Clinical Practice* published by Institute for Scientific Information, Philadelphia.

Pyelonephritis. (J. Buchanec *et al.*) *Acta Paediat. Acad. Sci. Hung.* 1974, **15**, 193.

Correlation between pyelonephritis and chronic tonsillitis. (A. V. Lyulko *et al.*) *Ther. Arch.* 1975, **46**, 73.

Diagnosis of chronic pyelonephritis. (N. A. Ratner *et al.*) *Ther. Arch.* 1975, **46**, 15.

Calculus pyonephrosis with *Candida albicans* infection. (M. J. Kelly and M. E. Mayo.) *Brit. J. Urol.* 1975, **47**, 130.

Three cases of pyonephrosis with perinephritic abscess. (A. Rometti and J. Boschi.) *J. Urol. Néphrol.* 1975, **81**, 263.

New features in the pathogenesis of renal tuberculosis and their significance for its detection. (A. L. Shabad.) *Urol. Int.* 1975, **30**, 297.

Der heutige Stand der operativen Behandlung in Nierentuberkulose. (The surgical treatment of renal tuberculosis in the present state.) (M. Pechestorfer *et al.*) *Acta Chir. Aust.* 1975, **7**, 4.

Evaluation of current therapeutic regimen for renal tuberculosis. (M. Wechsler and J. K. Lattimer.) *J. Urol.* 1975, **113**, 760.

Calculi. The relationship of the urinary cations, calcium, magnesium, sodium and potassium, in patients with renal calculi. (S. G. Welshman and M. G. McGeown.) *Brit. J. Urol.* 1975, **47**, 237.

Case of soft stones in the renal pelvis (J. Sikora *et al.*) *Z. KinderChir.* 1975, **17**, 78.

Ionized calcium and calcic renal lithiasis. (A. Macias *et al.*) *Rev. Clin. Esp.* 1975, **137**, 455.

Clinical concepts of renal calculous disease. (W. C. Thomas.) *J. Urol.* 1975, **113**, 423.

Medical evaluation of the patient with renal calculi. (E. P. Clerkin.) *Lahey Clinic Found. Bull.* 1975, **24**, 32.

Normocalcemic hyperparathyriodism, kidney stones and idiopathic hypercalciuria. (H. Johansson *et al.*) *Surgery*, 1975, **77**, 691.

The natural history of renal and ureteric calculi. (V. Marshall *et al.*) *Brit. J. Urol.* 1975, **47**, 117.

The residual renal stone. (M. Singh *et al.*) *Brit. J. Urol.* 1975, **47**, 125.

Calcium oxalate renal stones. (E. L. Prien.) *Ann. Rev. Med.* 1975, **26**, 173.

Recurrent calcic renal stones. Exploration pathogenesis, treatment. (J. Bernheim.) *Lyon Méd.* 1975, **233**, 706.

Mixed renal stone associated with multiple metabolic disorders. (A. Weinberger *et al.*) *Harefuah*, 1975, **88**, 320.

Parathormone levels in patients with recurrent calcium renal stones. (J. Bernheim *et al.*) *Nouv. Presse Méd.* 1975, **4**, 1913.

Effects of thiazides on serum and urinary zinc in patients with renal calculi. (M. Cobanim and E. R. Yendt.) *Amer. J. Med.* 1975, **58**, 137.

Indications for use of intestinal segments in management of nephrocalcinosis. (D. G. Skinner and W. E. Goodwin.) *J. Urol.* 1975, **113**, 436.

Anaesthesia considerations during nephrolithotomy with slush. (A. A. Birch and G. R. Mims.) *J. Urol.* 1975, **113**, 433.

Pediatric nephrolithiasis (R. S. Malek and P. P. Kelalis.) *J. Urol.* 1975, **113**, 545.

Renal lithiasis. (D. Wolff.) *Gaz. Méd. Franc.* 1975, **82**, 2061.

Nephrolithiasis or renal medullary cystic disease. (S. C. Morales *et al.*) *Rev. Clin. Esp.* 1975, **136**, 489.

Use of jugular vein catheterization and radioimmunological determination of parathyroid hormone in case of recurrent calcium nephrolithiasis. (J. Bernheim *et al.*) *J. Urol. Néphrol.* 1975, **81**, 299.

Circulatory Disorders. Giant aneurysm of the renal artery in a case of single kidney. Repaired by extracorporeal surgery followed by autotransplant. One year after healing. (J. P. Archimbaud *et al.*) *Chirurgie*, 1975, **101**, 408.

Acute renal artery occlusion. (P. Buri.) *Schweiz. Med. Wschr.* 1975, **105**, 941.

Evaluation of differential renal function studies in segmental renal artery occlusion. (A. Pfau *et al.*) *Brit. J. Urol.* 1975, **47**, 243.

Renal vascular resistance changes following thrombin-induced intravascular coagulation: role of platelet and fibrin emboli. (J. Høie.) *Acta Chir. Scand.* 1975, **141**, 167.

Renal artery aneurysms. (M. Lacombe *et al.*) *J. Chir.* 1974, **108**, 533.

Renal artery aneurysms. (E. F. Poulasse.) *J. Urol.* 1975, **113**, 443.

Anuria in remaining kidney due to unruptured iliac artery aneurysm. (L. Pedinielli *et al.*) *Chirurgie*, 1975, **101**, 52.

Aorta-renal artery bypass for renovascular hypertension. (J. Libertino and L. Zinman.) *Hosp. Pract.* 1975, **10**, 80.

Calcified renal artery aneurysm with arteriovenous fistula: report of a case. (M. Tabibi and L. Gottesman.) *J. Amer. Osteopath. Assoc.* 1975, **74**, 747/129.

Acute prolonged renal arterial infarction. Return of function after thromboendarterectomy. (P. K. Spanos *et al.*) *Amer. J. Surg.* 1975, **129**, 579.

Classification of essential arterial hypertension by determination of plasma renin activity. (M. Olmer *et al.*) *Helv. Chir. Acta*, 1975, **42**, 357.

Hypertension and unilateral hydronephrosis in children successfully treated by pyeloplasty: report of two cases. (W. S. Chapman and B. S. Douglas.) *J. Pediat. Surg.* 1975, **10**, 281.

The diagnostic of renal hypertension. (F. Bedos *et al.*) *J. Urol. Néphrol.* 1975, **81**, 15.

Surgical treatment of renal hypertension in children. (J. M. Kaufman *et al.*) *J. Urol.* 1975, **113**, 681.

Page kidney: correctable form of arterial hypertension. (G. Sufrin.) *J. Urol.* 1975, **113**, 450.

Renal artery hypertension: current diagnosis and treatment. (W. M. Kirkendall and M. Overturf.) *Texas Med.* 1975, **71**, 73.

Hypertension and renal artery stenosis with aneurysm formation in a solitary kidney in a patient with neurofibromatosis. (D. G. Hardy *et al.*) *Brit. J. Urol.* 1975, **47**, 137.

Hypertension due to renal artery stenosis in transplanted kidneys. (E. S. Lindsey *et al.*) *Ann. Surg.* 1975, **181**, 604.

Renal vein thrombosis in neonates. (J. F. Halvorsen and P. J. Moe.) *Acta Paediat. Scand.* 1975, **64**, 373.

Les thromboses veineuses rénales de l'adulte. [Renal vein thrombosis in adults.] *Schweiz. Med. Wschr.* 1975, **105**, 398.

Hypertension, renal vein thrombosis and renal failure (occurring in a patient on an oral contraceptive agent.) (G. L. Slick *et al.*) *Clin. Nephrol.* 1975, **3**, 70.

Thrombectomy for neonatal renal vein thrombosis. (I. M. Thompson *et al.*) *J. Urol.* 1975, **113**, 396.

Renal vein thrombosis following arteriography in a newborn. Treatment by urokinase. (J. L. Demarquez *et al.*) *Arch. Franc. Pédiat.* 1975, **32**, 381.

Renal vein thrombosis and nephrotic syndrome. (F. Llach *et al.*) *Ann. Intern. Med.* 1975, **83**, 8.

Reno-vascular surgery: experience of ten years on 80 cases. (A. Lantin *et al.*) *Union Méd. Canad.* 1975, **104**, 547.

Diagnostic approach to renovascular hypertension. (S. G. Sheps.) *Minn. Med.* 1975, **58**, 395.

Renovascular hypertension. (R. H. Dean and J. H. Foster.) *J. Ten. Med. Ass.* 1975, **68**, 379.

Takayasu arteritis as cause of renovascular hypertension. (G. Utz *et al.*) *Z. Kardiol.* 1975, **64**, 482.

Cysts. A case of suprarenal cyst. (J. F. Barault and C. Perrier.) *Lyon Chir.* 1975, **71**, 207.

Percutaneous management of renal cysts: results of a four-year study. (M. M. Raskin *et al.*) *Radiology*, 1975, **115**, 551.

Adrenal cyst associated with hypertension. (N. V. Raghavaiah and S. M. Singh.) *Brit. J. Urol.* 1975, **47**, 136.

Miscellaneous acquired cystic lesions of the kidney and retroperitoneum. (R. M. Friedenberg and R. M. Lilienfeld.) *Seminars Roentgen.* 1975, **10**, 155.

Simple cyst of the kidney. (J. A. Becker and M. Schneider.) *Seminars Roentgen.* 1975, **10**, 103.

Renal cystic disease—an overview. (M. Elkin.) *Seminars Roentgen.* 1975, **10**, 99.

The hydronephrotic type of unilateral congenital multicystic disease of the kidney. (B. Felson and L. J. Cussen.) *Seminars Roentgen.* 1975, **10**, 113.

Renal pseudocysts. (M. L. Sussman and A. Newman.) *Arizona Med.* 1975, **32**, 171.

Unilateral multicystic renal dysplasia. (H. Gamerman *et al.*) *J. Radiol. Electr.* 1975, **56**, 175.

"Septation sign" in multicystic dysplastic kidney. (R. S. Lachman *et al.*) *Pediat. Radiol.* 1975, **3**, 117.

Neoplasms. Normal radiological renal size: simple estimation from single urogram series. (A. M. Hunter *et al.*) *New Zeal. Med. J.* 1975, **81**, 409.

Radio diagnosis of acute renal abscess in adults. Early diagnosis in 7 cases. (V. Bismuth *et al.*) *J. Urol. Néphrol.* 1975, **81**, 197.

Radiological appearance of renal metastases. (G. Lemaitre *et al.*) *J. Radiol. Electr.* 1975, **56**, 505.

Squamous metaplasia of the renal pelvis. (M. L. Sussman and A. Newman.) *Arizona Med.* 1975, **32**, 472.

Unilateral renal agenesis associated with malignancy (S. B. Langundoye *et al.*) *E. Afr. Med. J.* 1975, **52**, 176.

Arteriography in metastatic neoplasms to the kidney. A report of three cases and a study of the literature. (J. Masselot *et al.*) *J. Radiol. Electr.* 1975, **56**, 119.

Renal venography in the evaluation of poorly vascularized neoplasms of the kidney. (J. C. Smith *et al.*) *Amer. J. Roentgen.* 1975, **123**, 552.

Phantom tumors of kidneys. (D. Hauri *et al.*) *Urologe*, 1975, **14**, 71.

Poorly vascularised renal tumors—clinical angiographical and histological findings. (L. Weissbach *et al.*) *Urologe*, 1975, **14**, 65.

The staging of renal parenchymal tumours. (S. Petković.) *Brit. J. Urol.* 1975, **47**, 13.

Erythroprotein production in renal tumors. (L. A. Kazal and A. J. Erslev.) *Ann. Clin. Lab. Sci.* 1975, **5**, 98.

Color scanning in topic and differential diagnosis of renal tumors. (A. V. Aivazyan.) *Vop. Oncol.* 1975, **21**, 24.

Surgical grand rounds: endocrine aspects of renal tumours. *Southern Med. J.* 1975, **68**, 481.

Renal and bladder malacoplakia resembling a tumour. (J. L'Hermite *et al.*) *J. Urol. Néphrol.* 1975, **81**, 213.

Renin-secreting renal tumour with severe hypertension. (O. S. Ørjavik *et al.*) *Acta Med. Scand.* 1975 **197**, 329.

The radiological diagnosis of "avascular" renal tumours. (F. W. Wright and M. M. Walker.) *Brit. J. Urol.* 1975, **47**, 253.

The pre-operative diagnosis of renal hamartoma. (R. W. McCallum.) *Clin. Radiol.* 1975, **26**, 257.

Renal medullary fibroma: report of case presenting as submucosal pelvic tumor. (K. W. Lennox and R. E. Clark.) *J. Urol.* 1975, **113**, 288.

Prostaglandins in human renal sarcoma—probable renomedullary interstitial cell sarcoma. (R. Drut and B. S. Decusminsky.) *Medicina*, 1975, **35**, 154.

Liposarcoma of the renal capsule in a 7 year old girl. (Y. Itzchak *et al.*) *Pediat. Radiol.* 1975, **3**, 182.

Renal carcinoma in pregnancy. (M. Pelosi *et al.*) *Obstet. Gynec.* 1975, **45**, 461.

Invasion of the gonadal vein in renal cell carcinoma. (F. M. Kelvin.) *Brit. J. Radiol.* 1975, **48**, 315.

Primary osteogenic carcinoma of the kidney. (A. Chambers and R. Carson.) *Brit. J. Radiol.* 1975, **48**, 316.

Solitary thyroid metastasis from clear-cell renal carcinoma. (P. Madore and S. Lan.) *Canad. Med. Ass. J.* 1975, **112**, 719.

Renal cell carcinoma. (J. A. Libertino and L. Zinman.) *Med. Clin. N. Amer.* 1975, **59**, 293.

Left to right shunt due to arteriovenous fistula formation in a renal cell carcinoma. (E. I. Curtiss *et al.*) *Arch Intern. Med.* 1974, **134**, 951.

Bilateral transitional cell carcinoma of renal pelvis with unilateral non-functioning kidney. (T. P. Bogaard and A. M. B. Goldstein.) *J. Urol.* 1975, **113**, 565.

Renal cell carcinoma presenting as right arterial tumor with successful removal using cardiopulmonary bypass. (J. G. Paul *et al.*) *Ann. Surg.* 1975, **181**, 471.

Transcatheter embolization of renal cell carcinoma. (H. M. Goldstein *et al.*) *Amer. J. Roentgen.* 1975, **123**, 557.

Renal cell carcinoma in the free wall of a simple renal cyst. (A. Srimannarayana *et al.*) *Brit. J. Urol.* 1975, **47**, 152.

Renal carcinoma in a cadaver kidney graft donor. (R. N. Baird *et al.*) *Brit. Med. J.* 1975, **2**, 371.

Diagnosis of renal cell carcinoma by use of new radiopharmaceutical. (A. T. Cole *et al.*) *J. Urol.* 1975, **113**, 711.

Bilateral renal-cell carcinomas (F. W. Wright.) *Radiology*, 1975, **115**, 543.

Natural history and staging of renal cell carcinoma. (J. M. Holland.) *C.A.*, 1975, **25**, 121.

Renin-secreting clear cell carcinoma of kidney. (J. W. Hollifield *et al.*) *Arch. Intern. Med.* 1975, **135**, 859.

Erythrocytosis and renal cell carcinoma with pulmonary metastases—case report with 18-year follow-up and brief discussion of literature. (V. Downing and S. Levine.) *Cancer*, 1975, **35**, 1701.

Regression of metastases after nephrectomy for renal cell carcinoma (S. J. Silber *et al.*) *Brit. J. Urol.* 1975, **47**, 259.

Resection of the vena cava for renal cell carcinoma: experimental studies on renoportal venous anastomosis. (F. Masuda *et al.*) *Jap. J. Urol.* 1975, **66**, 333.

Metastatic neonatal Wilms' tumor: a case report with review of the literature. (H. A. Wexler *et al.*) *Pediat. Radiol.* 1975, **3**, 179.

Unusual presentation in Wilms' tumour. (H. B. Eckstein.) *Z. KinderChir.* 1975, **16**, 426.

Capsular and vascular invasion: important prognostic factors in Wilms' tumor. (A. P. Mahesh Kumar *et al.*) *J. Pediat. Surg.* 1975, **10**, 301.

Nephroblastoma (Wilms' tumour). (M. G. Mott.) *Brit. J. Hosp. Med.* 1975, **13**, 161.

Ultrasound in differential diagnosis of Wilms tumors. (F. J. Helmig and H. Elser.) *Klin. Pädiat.* 1975, **187**, 278.

Advances in the treatment of Wilms' tumor. (J. A. Wolff.) *Cancer*, 1975, **35**, 901.

The congenital mesoblastic nephroma, benign embryoma or Wilms' pseudotumor. (L. G. Salisachs.) *Rev. Esp. Pediat.* 1975, **31**, 25.

Fever, lethargy and rash complicating treatment for Wilms' tumor—a new syndrome? (J. R. Cassady *et al.*) *Radiology*, 1975, **115**, 171.

The incipient Wilms' tumor. (J. R. Woodward *et al.*) *Pediat. Radiol.* 1975, **3**, 81.

Familial occurrence of Wilms's tumor: nephroblastoma in one of monozygous twins and in another sibling. (R. C. Juberg *et al.*) *Amer. J. Hum. Genet.* 1975, **27**, 155.

Syndrome of fetal gigantism, renal hamartomas and nephroblastomatosis with Wilms' tumor. (M. Perlman *et al.*) *Cancer*, 1975, **35**, 1212.

Wilms' tumor and renal cell carcinoma in retroperitoneal teratoma. (J. A. Carney.) *Cancer*, 1975, **35**, 1179.

Management of nephroblastoma in Kenya. (N. W. Awori and T. Norin.) *East Afr. Med. J.* 1975, **52**, 127.

Cystic partially differentiated nephroblastoma. (J. M. Brown.) *J. Path.* 1975, **115**, 175.

Indications for radiostatic and cytostatic therapy of nephroblastoma and sympathicoblastoma considering their multiple metastases. (H. Wurdinger *et al.*) *Röntgen-Bl. Klin. Prax.*, 1975, **28**, 174.

Cystic nephroblastoma in an adult. (G. Behr and M. Duari.) *Brit. J. Urol.* 1975, **47**, 268.

Mechanical Disorders. Use of a free graft of renal pelvis in treatment of obstructions of pelvi-ureteric junctions in childhood. (M. Pasini and I. Bradic.) *Z. KinderChir.* 1975, **16**, 433.

Renal function after release of chronic unilateral hydronephrosis in man. (J. Y. Gillenwater *et al.*) *Kidney Int.* 1975, **7**, 179.

Physiology and Experimental Observations. Caliceal urodynamics. (A. Puigvert.) *Urol. Int.* 1975, **30**, 282.

Clinicopathologic and experimental studies of myohemoglobinuric nephrosis. (Path. Res. Group Hospital of Fushun Mine Bureau.) *Chin. Med. J.* 1975, **1**, 257.

Study of the activity of blood serum of cholinesterase in diseases of the kidneys. (S. O. Androsova *et al.*) *Ther. Arch.* 1975, **46**, 62.

Ligation of renal vein in solitary kidney: effects on renal function. (D. L. McCullough and R. F. Gittes.) *J. Urol.* 1975, **113**, 295.

Effect of intrarenal furosemide on renal function and intrarenal hemodynamics in acute renal failure. (M. Epstein *et al.*) *Amer. J. Med.* 1975, **58**, 510.

Renal function abnormalities in post-unilateral ureteral obstruction in man: comparison of these defects to post-obstructive diuresis. (W. S. McDougal and L. Persky.) *J. Urol.* 1975, **113**, 601.

Renal Failure. Bilateral nephrectomy: analysis of 100 consecutive cases. (N. A. Viner *et al.*) *J. Urol.* 1975, **113**, 291.

The prescription of antibiotics in patients with renal failure. (P. Jungers *et al.*) *Sem. Hop.* 1975, **51**, 183.

Selective renal angiography in renal failure due to infection. (S. Arthachinta *et al.*) *Aust. Radiol.* 1975, **18**, 446.

Clinical determinants of survival from postoperative renal failure (S. M. Baek *et al.*) *Surg. Gynec. Obstet.* 1975, **140**, 685.

Free-water clearance patterns as predictors and therapeutic guides in acute renal failure. (S. M. Baek *et al.*) *Surgery*, 1975, **77**, 632.

Reduction in severity of acute renal failure in rats by beta-adrenergic blockade. (A. Iaina *et al.*) *Lancet*, 1975, **2**, 157.

Acute renal failure complicating ruptured abdominal aortic aneurysm. (S. K. Chawla *et al.*) *Arch. Surg.* 1975, **110**, 521.

Acute renal failure due to hyperuricaemia. (P. Paduart *et al.*) *Nouv. Presse Méd.* 1975, **4**, 1595.

Effect of prostaglandin A on acute renal failure in the rat. (R. F. Cioffi *et al.*) *Nephron*, 1975, **15**, 29.

Review of 60 cases of acute renal failure treated with hemodialysis. (E. M. de Heredia *et al.*) *Med. Clin.* 1975, **64**, 381.

Acute renal failure with extreme catabolism. (M. R. Kelly.) *U.S. Navy Med.* 1975, **65**, 26.

Acute renal failure during gentamicin treatment alone or associated with other antibiotics. Study of 6 cases. (L. R. Urioste *et al.*) *Rev. Clin. Esp.* 1975, **137**, 213.

Urography in acute renal failure. (W. R. Cattell and I. K. Fry.) *Amer. Heart J.* 1975, **90**, 124.

Acute renal failure in the post-traumatic patient. (D. Graham and R. Andersen.) *Minn. Med.* 1975, **58**, 529.

Plan for acute renal failure. (R. S. Dobrin.) *Drug Ther.* 1975, **5**, 79.

Increased incidence of malignancy during chronic renal failure. (A. J. Matas *et al.*) *Lancet*, 1975, **1**, 883.

Impotence in patients with chronic renal failure on dialysis: its frequence and etiology. (F. P. Sherman.) *Fertil. Steril.* 1975, **26**, 221.

Sexual function in patients with chronic renal failure. (H. S. Abram *et al.*) *J. Nerv. Ment. Dis.* 1975, **160**, 220.

Use of co-trimoxazole in chronic renal failure. (R. R. W. Tasker *et al.*) *Lancet*, 1975, **1**, 1216.

Transplantation. Renal failure after transplantation. (Washington University School of Medicine.) *Amer. J. Med.* 1975, **58**, 537.

Determination of the optimum temperature for regional renal hypothermia during temporary renal ischaemia. (J. P. Ward.) *Brit. J. Urol.* 1975, **47**, 17.

Thrombocytopenia in extracorporeal circulation (ECC). 2. Bubble oxygenator versus artificial kidney. (J. C. F. Dejong *et al.*) *Trans. Amer. Soc. Artif. Intern. Organs*, 1975, **21**, 40.

Improved renal allograft survival using mixed lymphocyte culture for selection of nonidentical living related donors. (R. R. Riggio *et al.*) *Trans Amer. Soc. Artif. Intern. Organs*, 1975, **21**, 90.

Continuous single pass perfusion of isolated kidney. (S. P. Auda *et al.*) *Trans. Amer. Soc. Artif. Intern. Organs*, 1975, **21**, 84.

Pediatric renal transplantation. (Y. B. Talwalkar *et al.*) *Western J. Med.* 1975, **123**, 1.

Kidneys for transplantation. *Lancet*, 1975, **2**, 164.

Kidney donation—pressing need in the treatment of end stage renal failure. (J. Colberg and N. Lasker.) *Penn. Med.* 1975, **78**, 52.

Kidney transplants and the law; coroners and manslaughter. *Brit. Med. J.* 1975, **3**, 108.

Fallopian tube as ureteral substitute in a living donor renal allograft. (R. E. Duncan and A. T. Evans.) *Brit. J. Urol.* 1975, **47**, 300.

A comparison of cryoprecipitated plasma and albumin solutions for machine preservation of ischaemically damaged canine kidneys. (A. G. R. Sheil *et al.*) *Aust. N. Zeal. J. Surg.* 1974, **44**, 412.

Continuous perfusion of human cadaveric kidneys for transplantation. (T. P. Stephenson *et al.*) *Brit. J. Urol.* 1975, **47**, 37.

Predictive parameters for renal preservation. (E. A. Santiago-Delpin *et al.*) *Trans. Amer. Soc. Artif. Intern. Organs*, 1974, **20**, 550.

Hyperosmolar cold storage kidney preservation solution. (J. Y. Masuda *et al.*) *Amer. J. Hosp. Pharm.* 1975, **32**, 397.

Preservation of the kidney: comparative efficacy of two simple perfusion techniques. (J. Dauchel *et al.*) *J. Chir.* 1975, **109**, 387.

Factors determining early kidney function following clinical preservation. (L. H. Toledo-Pereyra *et al.*) *Minn. Med.* 1975, **58**, 446.

Role of juxtaglomerular apparatus in renal allograft rejection (M. J. Varkarakis and G. P. Murphy.) *New York J. Med.* 1975, **75**, 629.

Useful functioning of "non-functioning" renal homograft. (D. J. Shapiro *et al.*) *Brit. Med. J.* 1975, **3**, 140.

Renal transplantation: trends and prospects. (D. J. H. Fisher *et al.*) *Brit. J. Hosp. Med.* 1975, **13**, 451.

Ultrasonic testing in the evolution of renal transplantations. (M. Rabadan *et al.*) *Rev. Clin. Esp.* 1975, **137**, 327.

Renal autotransplantation using hypothermic storage and pulsatile perfusion. (A. G. Diethelm *et al.*) *J. Urol.* 1975, **113**, 755.

Blood flow changes induced by transplantation of kidney in iliac vessels. (R. V. Navarrete *et al.*) *Rev. Clin. Esp.* 1975, **137**, 139.

Ultrasound in the diagnosis of fluid collections following renal transplantation. (P. Morley *et al.*) *Clin. Radiol.* 1975, **26**, 199.

Preanastomotic arterial stenosis in renal transplant recipients. A report of four cases. (L. Frödin *et al.*) *Scand. J. Urol. Nephrol.* 1975, **9**, 66.

Early spontaneous rupture of a renal transplant. Conservative surgical treatment with a three and half year follow-up. (J. P. Sarramon *et al.*) *J. Urol. Néphrol.* 1975, **81**, 39.

Arterial stenosis complicating renal allotransplantation in man: a study of 38 cases. (M. Lacombe.) *Ann. Surg.* 1975, **181**, 283.

Extravesical ureteroneocystostomy in 170 renal transplant patients. (J. W. Konnak *et al.*) *J. Urol.* 1975, **113**, 299.

Gastro-duodenal ulcer in kidney-transplanted patients receiving immunosuppressive treatment. (K. Rasmussen *et al.*) *Acta Chir. Scand.* 1975, **141**, 61.

Cystography after kidney transplantation. (R. Metyš *et al.*) *Radiol. Clin.* 1975, **44**, 172.

Lymphocele: a significant complication following renal transplantation. (W. S. Lorimer *et al.*) *Lymphology*, 1975, **8**, 20.

Problems of infections following renal transplantation (P. Schmidt *et al.*) *Wien. Klin. Wschr.* 1975, **87**, 367.

Postanastomotic renal-artery stenosis after renal transplantation. (H. Wilms *et al.*) *Deutsch. Med. Wschr.* 1975, **100**, 1376.

Seminoma in renal transplant recipient. (R. E. Nellans and J. Ravera.) *J. Urol.* 1975, **113**, 871.

Spontaneous rupture of renal transplants. (J. A. Libertino *et al.*) *Lahey Clin. Foundation Bull.* 1975, **24**, 111.

Investigatory Procedures. The role of ultrasound in the diagnosis of renal mass lesions. (M. T. Hogan *et al.*) *W. Virginia Med. J.* 1975, **71**, 135.

B-mode ultrasound scanning in the diagnosis of renal lesions. (J. N. Bloom *et al.*) *Amer. J. Surg.* 1975, **129**, 636.

Kidney depth measurements using a double isotope technique. (S. T. Ostrowski and P. Tothill.) *Brit. J. Radiol.* 1975, **48**, 291.

A method for universal punched-tape recording of time-activity curves and its use in isotope nephrography. (R. Dietrich *et al.*) *Radiobiol. Radiother.* 1975, **16**, 130.

Computer evaluation of isotope nephrograms (part I). (G. Esther.) *Radiobiol. Radiother.* 1975, **16**, 65.

A comparison between urography and radioisotope renography in the follow-up of surgery for hydronephrosis. (B. Otnes *et al.*) *Scand. J. Urol. Nephrol.* 1975, **9**, 50.

Renal toxicity of contrast dyes used for pyelography. (M. Tremblay and J. Bernheim.) *Lyon Méd.* 1975, **233**, 1019.

Radiation dose measurements in intravenous pyelography. (M. Egeblad and E. Gottlieb.) *Ann. Radiol.* 1975, **18**, 321.

Renal imaging in M-99 TC-polyphosphate bone scanning—focal increased renal uptake in metastatic carcinoma of lung. (P. M. Fitzer.) *J. Nucl. Med.* 1975, **16**, 602.

Ferromagnetic silicone necrosis of hypernephromas by selective vascular occlusion to tumor: new technique. (R. D. Turner *et al.*) *J. Urol.* 1975, **113**, 455.

On radiological representation of the renal veins. (H. Platzbecker *et al.*) *Radiol. Diagn.* 1974, **15**, 465.

The capsule sign in severe hydronephrosis. (G. Lemaitre and P. Meaux.) *J. Radiol. Electr.* 1975, **56**, 205.

B-Mode ultrasound scanning in the diagnosis of renal lesions. (J. N. Bloom *et al.*) *Amer. J. Surg.* 1975, **129**, 636.

The use of echotomography in the diagnosis of large kidneys in children. (G. Faure *et al.*) *J. Urol. Néphrol.* 1975, **81**, 432.

Angiocinedensitometry of the kidney. (H. K. Deininger.) *Fortschr. Med.* 1975, **93**, 523.

Kidney position and the measurement of relative uptake of ^{131}hippuran in renography. (C. C. Nimmon *et al.*) *Brit. J. Radiol.* 1975, **48**, 286.

Paediatric renal masses: some experiences with ultrasound and arteriography. (B. J. Cremin.) *S. Afr. Med. J.* 1975, **49**, 731.

Echography and the kidney remaining silent at I.V.U. (M. Bittard *et al.*) *J. Med. Strasbourg*, 1975, **6**, 161.

Diagnosis and treatment of expansive processes of kidneys. (G. Vanregemorter.) *Helv. Chir. Acta*, 1975, **42**, 407.

Value of fine needle aspiration biopsy and intravenous pyelography in diagnosis of renal masses. (P. Thommesen and B. Nielsen.) *Fortschr. Röntgen.* 1975, **122**, 248.

Technique and results of fifty-five open renal biopsies in children. (J. D. Burrington.) *Surg. Gynec. Obstet.* 1975, **140**, 613.

Ultrasonic localization for renal biopsy. (B. B. Goldberg *et al.*) *Radiology*, 1975, **115**, 167.

Angiographic injection of clot for hemorrhage after renal biopsy. (S. J. Silber and R. E. Clark.) *New Eng. J. Med.* 1975, **292**, 1387.

Late presenting intrarenal haematoma as a complication of renal biopsy. (A. G. Hocken and J. N. Killie.) *New Zeal. Med. J.* 1975, **81**, 483.

Spontaneous renal subcapsular hematoma renal angiography as a diagnostic aid. (S. Choi and E. Jennings.) *J. Surg. Oncol.* 1975, **7**, 1.

Estimation of renal size from radiographs: is the effort worthwhile? (G. J. Griffiths *et al.*) *Clin. Radiol.* 1975, **26**, 249.

Nonvisualization or nonfunctioning of one kidney on intravenous pyelogram. (J. M. Korsower and M. M. Reeder.) *J.A.M.A.*, 1975, **232**, 746.

Usefulness of ultrasound in evaluation of renal masses in adults. (E. H. Smith and A. H. Bennett.) *J. Urol.* 1975, **113**, 525.

Adverse reactions to intravenous pyelography in children. (C. A. Gooding *et al.*) *Amer. J. Roentgen.* 1975, **123**, 802.

Operative Procedures. Some technical considerations on partial nephrectomy. (C. Filimon *et al.*) *J. Urol. Néphrol.* 1975, **81**, 385.

An incision for *en bloc* nephrectomy. (G. F. Cassie.) *Brit. J. Surg.* 1975, **62**, 565.

Surgical renal biopsy through posterior lumbar incision. Our experience of 100 cases. (G. Faure *et al.*) *J. Urol. Néphrol.* 1975, **81**, 49.

An unusual complication of endoscopic extraction of a pelvic calculus: rupture of the renal pelvis. (B. Dufour.) *J. Urol. Néphrol.* 1975, **81**, 76.

Conservative renal surgery for adenocarcinoma. The place of bench surgery. (J. E. A. Wickham *et al.*) *Brit. J. Urol.* 1975, **47**, 25.

Laboratory and clinical experience with extracorporeal renal surgery. (R. J. Krane *et al.*) *Trans. Amer. Soc. Artif. Intern. Organs*, 1974, **20**, 538.

Renal parenchyma resection—development, technique, problems. (H. D. Nöske.) *München. Med. Wschr.* 1975, **117**, 817.

Delayed peritoneal-cutaneous fistula; a complication of bilateral nephrectomy. (N. K. Bissada *et al.*) *Brit. J. Urol.* 1975, **47**, 262.

Iatrogenic complication of nephrostomy. (T. T. Alagaratnam and C. H. Leong.) *J. Urol.* 1975, **113**, 286.

Easy and safe technique for nephrostomy. (C. H. Kim and O. C. Fjeldborg.) *Surg. Gynec. Obstet.* 1975, **141**, 95.

Late results of nephropexy for nephroptosis according to a new indication schema. (G. Ludwig *et al.*) *Deutsch. Med. Wschr.* 1975, **100**, 1501.

URETER

General. The ureter after total cystectomy. (R. Küss *et al.*) *J. Urol. Néphrol.* 1975, **81**, 406.

Reversible ureteral stenosis as a delayed complication of operation on colon and rectum. (B. Klevmark, and K. Nygaard.) *Acta Chir. Scand.* 1975, **141**, 153.

Anuria and renal colic revealing ureteral metastases from uterine carcinoma. (G. Patoir *et al.*) *J. Urol. Néphrol.* 1975, **81**, 149.

Congenital Anomalies. Retrocaval ureter. (N. Shah and I. Spence.) *Int. Surg.* 1975, **60**, 364.

Retrocaval ureter with carcinoma of the renal pelvis: report of a case. (K. Sagami *et al.*) *Int. Urol. Nephrol.* 1975, **7**, 49.

Nonobstructive circumcaval (retrocaval) ureter: a report of 2 cases. (J. E. Crosse *et al.*) *Radiology*, 1975, **116**, 69.

Tubular duplication of rectum with rectourethral fistula. (R. S. Waldbaum and A. F. Glendinning.) *J. Urol.* 1975, **113**, 876.

Retrocaval ureter and crossed dystopia in solitary kidney. (I. Krause and G. Phiebl.) *Zbl. Chir.* 1975, **100**, 503.

Obstruction of lower ureteral segment caused by vascular anomalies. (S. Scultety and B. Varga.) *Urologe*, 1975, **14**, 144.

The congenital refluxing megaureter: experiences with surgical reconstruction. (J. H. Johnston and A. Farkas.) *Brit. J. Urol.* 1975, **47**, 153.

Ectopic ureterocoele and its treatment. (H. Lipsky and F. Eppich.) *Wien. Klin. Wschr.* 1975, **87**, 272.

Supralevator imperforate anus with unusual associated anomalies colonic ureteral ectopy intraluminal calcified meconium. (A. H. Felman *et al.*) *Pediat. Radiol.* 1975, **3**, 78.

Diagnosis and treatment of ectopic ureter. (P. Dziuba *et al.*) *Z. KinderChir.* 1975, **16**, 192.

Trauma. Ureteral and periureteral fibrosis as delayed sequelae to lower urinary tract injury. (M. S. Rao *et al.*) *J. Urol.* 1975, **113**, 610.

A rare ureteral injury secondary to lumbar sympathetic ganglion block with phenol (S. S. Ambasta.) *Brit. J. Urol.* 1975, **47**, 276.

Psoas-bladder hitch procedure: our experience with repair of injured ureter in men. (S. V. Kishev.) *J. Urol.* 1975, **113**, 772.

Ureteral and bladder injuries in children. (J. P. Donohue.) *Pediat. Clin. N. Amer.* 1975, **22**, 393.

Bilateral pelvi-ureteric avulsion following closed trauma. (V. E. Boston and B. T. Smyth.) *Brit. J. Urol.* 1975, **47**, 149.

Surgical injuries of the ureter. A review of 42 cases. (I. Ihse *et al.*) *Scand. J. Urol. Nephrol.* 1975, **9**, 39.

Ureteral lesions due to bullet wound. Means of exploration and management. (M. Sarramon and J. Serby.) *J. Urol. Néphrol.* 1975, **81**, 144.

Fistula. Uretero-vaginal fistula, clinical and operative observations. (H. A. Amin.) *J. Kuwait Med. Ass.* 1975, **9**, 65.

Idiopathic ureteroduodenal fistula. (H. Shiozaki *et al.*) *J. Urol.* 1975, **113**, 714.

Traumatic arterio-ureteral fistula: "hematuria" without urine. (C. Dang and M. J. Sullivan.) *J. Trauma*, 1975, **15**, 361.

Infections. Renal and retrovesical hydatidosis—effects of renal hydatid cysts on ureter. (M. Pavonemacaluso *et al.*) *Helv. Chir. Acta*, 1975, **42**, 367.

The tuberculosis of the ureter. (H. Heidler *et al.*) *Acta Chir. Aust.* 1975, **7**, 56.

Calculi. Complications of surgical and endoscopic treatment of ureteral lithiasis. (D. Wolff *et al.*) *J. Urol. Néphrol.* 1975, **81**, 61.

Ureteral calculi: review of 17 years of experience at community hospital. (H. H. Henry and E. M. Tomlin.) *J. Urol.* 1975, **113**, 762.

Ureteral calculus in pregnancy and the puerperium. (J. Zerner.) *J. Maine Med. Ass.* 1975, **66**, 151.

Giant ureteric calculus (N. Ananthakrishnan and B. M. L. Kapur.) *Aust. New Zeal. J. Surg.* 1975, **45**, 74.

Ureteral lithiasis (J. Neveu.) *Sem. Hop.* 1975, **51**, 1363.

Oxyphenbutazone in the treatment of acute ureteral stone disease. (A. Nygård and S. Bjorneby.) *Scand. J. Urol. Nephrol.* 1975, **9**, 36.

Recurrent calcium phosphate ureteral calculi—a red flag. (M. J. V. Smith.) *J.A.M.A.*, 1975, **232**, 549.

Complications arising from the treatment of ureteral lithiasis. (L. Quénu.) *J. Urol. Néphrol.* 1975, **81**, 125.

Ureteral calculi treated by the endoscopic route or by laparotomy over the last ten years. (J. Lange *et al.*) *J. Urol. Néphrol.* 1975, **81**, 112.

Incidents and complications of treatment of ureteral calculi. Review of 650 case records. (H. Navratil and D. Grasset.) *J. Urol. Néphrol.* 1975, **81**, 119.

Complications of endoscopic and surgical treatment of ureteral calculi. (M. Bittard *et al.*) *J. Urol. Néphrol.* 1975, **81**, 107.

Complications of operations for ureteral lithiasis. (G. Patoir *et al.*) *J. Urol. Néphrol.* 1975, **81**, 122.

Discussion on the complications of treatment of ureteral calculi. (J. Auvert.) *J. Urol. Néphrol.* 1975, **81**, 130.

Complications of surgical and endoscopic operations for ureteral calculus. (E. Mazeman and L. Wemeau.) *J. Urol. Néphrol.* 1975, **81**, 127.

Incidents and complications of treatment of ureteral lithiasis. Therapeutic consequences. (A. Lhez.) *J. Urol. Néphrol.* 1975, **81**, 116.

Iatrogenic complications of surgery of calculi of the terminal ureter. (A. Steg *et al.*) *J. Urol. Néphrol.* 1975, **81**, 92.

Complications of surgical and endoscopic treatment of calculi of the pelvic ureter. (A. Le Duc and M. Camey.) *J. Urol Néphrol.* 1975, **81**, 96.

Incidents and complications of ureteral lithiasis. Report of 395 cases. (Cl. Bollak *et al.*) *J. Urol. Néphrol.* 1975, **81**, 82.

Three cases with severe complications following treatment of ureteral calculi. (R. Ballanger.) *J. Urol. Néphrol.* 1975, **81**, 70.

New approach to endoscopic treatment of calculi of the ureter. (G. Bertrand, report by M. Camey.) *J. Urol. Néphrol.* 1975, **81**, 99.

Retro-peritoneal collections of urine, a rare complication of the surgical treatment of calculi of the lumbo-iliac ureter. (B. Dufour *et al.*) *J. Urol. Néphrol.* 1975, **81**, 72.

Extraction of ureteral calculi with Dormia's catheter. Indications and complications. (L. Lafrance.) *J. Urol. Néphrol.* 1975, **81**, 101.

Trial of prevention of complications of surgical treatment of ureteral calculi. (P. Guillemin *et al.*) *J. Urol. Néphrol.* 1975, **81**, 90.

Neoplasms. Primary carcinoma of the ureter—prognostic study. (M. A. Batata *et al.*) *Cancer*, 1975, **35**, 1626.

Ureteral carcinoma in situ. (D. G. Linker and W. F. Whitmore.) *J. Urol.* 1975, **113**, 777.

Concerning a secondary malignant tumour of the ureter. (J. Ramiara and J. Courant.) *Méd. Armées*, 1975, **3**, 456.

Aspetti di patologia vesico-ureterale dopoisterectomia radicale addominale e vaginale per cancro cervicale uterino. (L. De Cecco *et al.*) *Minerva Ginec.* 1975, **27**, 193.

Renal autotransplantation and partial resection of ureter for recurrent benign ureteral tumor. (E. C. Saltzstein and S. W. Fine.) *Surgery*, 1975, **77**, 607.

Physiology. Ultrastructural evidence for adrenergic and cholinergic innervation of human ureter. (C. C. Schulman.) *J. Urol.* 1975, **113**, 765.

Physiology and physiopathology of the ureter. (R. L. Vereecken.) *Acta Urol. Belg.* 1975, **43**, 113.

Mechanical Disorders. Rare case of ureteric stenosis. (G. Benz.) *Z. KinderChir.* 1975, **16**, 451.

Severe sub-pyelic stenosis of the ureter after removal of a calculus from the pyelo-ureteral junction, treated by total uretero-ileoplasty. (J. Caissel.) *J. Urol. Néphrol.* 1975, **81**, 78.

Familial occurrence of nonobstructive, noninfectious vesicoureteral reflux with renal scarring. (P. R. Lewy and A. B. Belman.) *J. Pediat.* 1975, **86**, 851.

Surgical management of vesicorenal reflux in children. (Ch. Viville *et al.*) *J. Med. Strasbourg*, 1975, **6**, 69.

Intrarenal reflux and its relationship to renal scarring. (J. S. Rose *et al.*) *J. Urol.* 1975, **113**, 400.

Vesicoureteral reflux and renal scarring. (B. R. Girdany.) *J. Pediat.* 1975, **86**, 998.

Ureteral reflux in infancy. (C. D. Vermillion *et al.*) *Rocky Mountain Med. J.* 1975, **72**, 200.

Role of scheduled voiding in management of primary vesicoureteral reflux. (E. Leiter.) *J. Urol.* 1975, **113**, 686.

Family study of vesicoureteral reflux. (H. C. Bredin *et al.*) *J. Urol.* 1975, **113**, 623.

Vesicoureteral reflux: etiology, significance and management. (J. L. Weinerth and J. F. Glenn.) *North Carolina Med. J.* 1975, **36**, 223.

^{131}I Hippuran quantitative scintillation camera studies in evaluation and management of vesicoureteral reflux. (B. B. Evans *et al.*) *J. Urol.* 1975, **113**, 404.

Experiences and late results in treatment of vesicoureteral reflux according to Politano-Leadbetter. (W. H. Weiske and G. Bopp.) *Z. KinderChir.* 1975, **16**, 153.

Primary obstructive megaureter in adults. (M. K. Hanna and J. K. Wyatt.) *J. Urol.* 1975, **113**, 328.

Iliac artery aneurysm: common cause of ureteral obstruction. (R. Safran *et al.*) *J. Urol.* 1975, **113**, 605.

Total obstruction of an ureteral prosthesis. (J. de Leval and Ch. Maquinay.) *Acta Urol. Belg.* 1975, **43**, 5.

Nature of the acidifying defect after the relief of ureteral obstruction. (J. Walls *et al.*) *Kidney Int.* 1975, **7**, 304.

Pelvic endometriosis and ureteral obstruction. (C. F. Langmade.) *Amer. J. Obstet. Gynec.* 1975, **122**, 463.

Ureteral obstruction secondary to aortic femoral by-pass. (L. Vereecken *et al.*) *Acta. Chir. Belg.* 1975, **74**, 382.

Anuria resulting from extrinsic ureteral compression. (D. L. Dalton *et al.*) *Southern Med. J.* 1975, **68**, 711.

Analgesic abuse, ureteric obstruction and retroperitoneal fibrosis. (C. T. Lewis *et al.*) *Brit. Med. J.* 1975, **2**, 76.

Ureteric obstruction due to sigmoid diverticulitis. (B. J. Rees and P. M. Bolton.) *Brit. J. Surg.* 1975, **62**, 247.

Investigatory Procedures. Ureterometrographic studies on human subjects with normal urinary tract system. (M. Tabatabai and R. Kadivar.) *Brit. J. Urol.* 1975, **47**, 263.

Operative Procedures. Case against incorporation of bowel segments into closed urinary system. (E. A. Tanagho.) *J. Urol.* 1975, **113**, 796.

Reimplantation of the ureter on the bladder. (L. Boccon-Girod *et al.*) *J. Urol. Néphrol.* 1975, **81**, 412.

Studies on action potentials of the upper urinary tract IV. The effects of complete transection of the ureter and its recommunication between upper and ureteral orifice using a vinyl catheter upon the action potentials and intraluminal pressure of the ureter in mongrel dogs. (T. Akasaka *et al.*) *Jap. J. Urol.* 1975, **66**, 327.

Surgical correction of ureteral disturbances of excretion using a gamma surgical camera. (H. Kucera *et al.*) *Z. Gynäk.* 1975, **97**, 361.

Ureterostomy-in-situ. (R. R. A. Syme.) *Aust. New Zeal. J. Surg.* 1975, **45**, 69.

Vesicoureteroplasty in paraplegic: long-term follow-in 77 patients. (R. W. Reece and R. H. Hackler.) *J. Urol.* 1975, **113**, 474.

Complications of transureteroureterostomy. (R. M. Erlich and D. G. Skinner.) *J. Urol.* 1975, **113**, 467.

Useful applications of transureteroureterostomy in adults and children. (W. Brannan.) *J. Urol.* 1975, **113**, 460.

On a long-standing case of ureteral replacement. (F. X. de Preux and W. von Niederhäusern.) *Ann. Urol.* 1975, **9**, 17.

Ureteral substitute by fallopian tube. Experimental study. (B. Vidne *et al.*) *Urol. Int.* 1975, **30**, 173.

The effect of transuretero-ureterostomy upon conduction of peristaltic waves: an electro-ureterographic study. (T. Harata.) *Jap. J. Urol.* 1975, **66**, 91.

Clinical and experimental studies on ureteroneocystostomy by means of the modified triangular flap method. (K. Saito.) *Jap. J. Urol.* 1975, **66**, 68.

Complications of ureterotomy. (J. Ducassou *et al.*) *J. Urol. Néphrol.* 1975, **81**, 109.

The present position in complications of surgery of the ureter. (M. Le Guillou *et al.*) *J. Urol. Néphrol.* 1975, **81**, 102.

Impaction of Dormia's catheter. (D. Berge.) *J. Urol. Néphrol.* 1975, **81**, 88.

BLADDER

General. Study concerning the late reaction of the urinary bladder following irradiation of the carcinoma of the cervix. (H. J. Kümper *et al.*) *Strahlentherapie*, 1975, **149**, 602.

The herald lesion of the urinary bladder: a non-specific but significant pathologic change. (M. M. Melicow and A. C. Uson.) *Hum. Path.* 1975, **6**, 270.

Primary hydatid cyst of the bladder. (H. K. Fuloria *et al.*) *Brit. J. Urol.* 1975, **47**, 192.

Effects of inguinal hernias upon the bladder and ureters. (R. R. Goldin and R. A. Rosen.) *Radiology*, 1975, **115**, 55.

Nitrogen metabolism in bears: urea metabolism in summer starvation and in winter sleep and role of urinary bladder in water and nitrogen conservation. (R. A. Nelson.) *Mayo Clinic Proc.* 1975, **50**, 141.

Congenital Anomalies. Genital aspects of exstrophy. (J. H. Johnston.) *J. Urol.* 1975, **113**, 701.

Role of older methods of management in bladder problems in spina bifida. (E. Pekarovic *et al.*) *Z. KinderChir.* 1975, **17**, 60.

Vesical exstrophy operated by Lattimer's technic: 10 years results. (J. Cibert and J. Cibert.) *J. Urol. Néphrol.* 1975, **81**, 45.

Infections and Cystitis. Direct and indirect radionuclide cystography. (J. J. Conway *et al.*) *J. Urol.* 1975, **113**, 689.

Extra-luminal barium escape following double contrast cystography (details of one complication). (R. H. Wiggers and G. Rosenbusch.) *Forstschr. Röntgen.* 1975, **122**, 467.

Empyema cystitis treated by intermittent self-catheterization. (K. R. Hertwig.) *J. Urol.* 1975, **113**, 719.

Condylomata acuminata of the bladder. (H. V. Nielsen.) *Scand. J. Urol. Nephrol.* 1975, **9**, 169.

Cystitis emphysematosa. (D. Sunaric.) *Fortschr. Röntgenstr.* 1975, **122**, 550.

Control of refractory vesical haematuria by selective vesical embolisation. Seven cases of radiation cystitis and recurrent tumours. (M. le Guillou *et al.*) *Nouv. Presse Med.* 1975, **4**, 1703.

Schistosomiasis of the urinary bladder. (R. B. Roy and M. J. Hayward.) *Brit. J. Vener. Dis.* 1975, **51**, 134.

Clinicopathological conference—Fifty seven year old male with symptoms of chronic cystitis. (A. J. Hartzell and J. F. Balow.) *South Dakota J. Med.* 1975, **28**, 17.

Calculi. Bladder stone in childhood. (P. Naysan *et al.*) *New York J. Med.* 1975, **75**, 1288.

Bladder stone. *Brit. Med. J.* 1975, **2**, 578.

Hanging bladder stone formed around Mersilene mesh. (P. P. Dongaonkar.) *Brit. J. Surg.* 1975, **62**, 413.

Diverticulum. Fibrosarcoma arising in diverticulum of the urinary bladder. (V. M. Doctor and D. K. Karanjavala.) *Brit. J. Urol.* 1975, **47**, 184.

Neoplasms. Embryonal rhabdomyosarcoma of bladder and prostate in childhood. (J. W. Timmons *et al.*) *J. Urol.* 1975, **113**, 694.

Grave complications of bladder papillomata. (L. Quénu.) *Chirurgie*, 1975, **101**, 466.

Bladder cancer mortality in diabetics in relation to saccharin consumption and smoking habits. (B. Armstrong and R. Doll.) *Brit. J. Prev. Soc. Med.* 1975, **29**, 73.

Importance of inflammation before, during and after termination of radiation therapy of malignant tumours in urinary bladder. (J. Arndt *et al.*) *Radiobiol. Radiother.* 1974, **15**, 591.

Observations on possible autoimmune therapeutic effects in experimentally produced rat bladder tumors. (B. Fingerhut and R. J. Veenema.) *Urol. Int.* 1975, **30**, 255.

Ultrasound in the staging of bladder tumours. (I. S. McLaughlin *et al.*) *Brit. J. Urol.* 1975, **47**, 51.

Chemotherapy for bladder tumours. (M. Pavone-Macaluso *et al.*) *Gaz. Med. Franc.* 1975, **82**, 1365.

Late effects of transurethral resection of bladder tumors at the ureteric orifice. (A. Gottfries *et al.*) *Scand. J. Urol. Nephrol.* 1975, **9**, 32.

Treatment of multiple superficial papillary tumors of bladder by intracavitary Yttrium-90. (K. R. Durrant and A. H. Laing.) *J. Urol.* 1975, **113**, 480.

Induction of bladder tumours in the mouse by direct implantation of 20-methyl-cholanthrene. (O. Campobasso *et al.*) *Tumori*, 1975, **61**, 17.

New cryotherapeutic probe with interchangeable optical system for transurethral treatment of bladder tumors. (A. Sigel.) *Urologe*, 1975, **14**, 156.

Fractionated cystography to assess infiltration of the bladder wall by intravesical tumors. (J. L. Sakkas *et al.*) *Int. Surg.* 1975, **60**, 273.

Studies on urinary isozymes of lactic dehydrogenase and β-glucuronidase in patients with bladder tumors. (Y. Motomiya *et al.*) *Urol. Res.* 1975, **3**, 41.

Current results from treatment of bladder tumors with total cystectomy at Roswell Park Memorial Institute. (Z. Wajsman *et al.*) *J. Urol.* 1975, **113**, 806.

Carcinoma of the bladder with positive cytological smear 7 years before the tumour became clinically obvious. (E. Benassayag *et al.*) *J. Urol. Néphrol.* 1975, **81**, 466.

Carcinoma in situ of the bladder. Three cases. (This paper will appear later as an original article.) (A. Steg and J. P. Desgrez.) *J. Urol. Néphrol.* 1975, **81**, 468.

Cutaneous metastases from carcinoma of the urinary bladder. (T. R. Bedi and L. K. Bhutani.) *Int. Surg.* 1975, **60**, 170.

Carcinoma of the bladder—limitation and reasons for failure of radical cystectomy. (F. H. Schroder and W. Jellinghaus.) *Urologe*, 1975, **14**, 60.

Preoperative radiotherapy of the carcinoma of the bladder. (H. Ernst *et al.*) *Strahlentherapie* 1975, **149**, 341.

A clinical evaluation of hydrostatic pressure treatment for carcinoma of the bladder. (G. B. Coombes.) *Brit. J. Urol.* 1975, **47**, 177.

Familial transitional cell carcinoma of bladder. (D. L. McCullough *et al.*) *J. Urol.* 1975, **113**, 629.

Cytology of urine with respect to operative treatment of bladder carcinoma. (D. Volter and H. Ziegler.) *Aktuel. Urol.* 1975, **6**, 83.

A correlative cytohistologic study on the interrelationship between exfoliated urinary bladder carcinoma cell types and staging and grading of these tumors. (H. Suprun and W. Bitterman.) *Acta Cytol.* 1975, **19**, 265.

ATP-ase activity of lymphocytes from patients with carcinomas of the urinary bladder. (J. Ellegaard *et al.*) *Scand. J. Urol. Nephrol.* 1975, **9**, 105.

Carcinoma within bladder diverticula. (P. Sanidad *et al.*) *Illinois Med. J.* 1975, **147**, 538.

Prognosis of bladder carcinoma in patients treated with cystectomy. (M. J. Varkarakis *et al.*) *Int. Urol. Nephrol.* 1975, **7**, 39.

Osteogenic sarcoma of the bladder. (J. Murat *et al.*) *J. Chir.* 1975, **109**, 327.

Early diagnosis of cancer of the bladder. (V. Lent.) *Deutsch. Med. Wschr.* 1975, **100**, 902.

Bladder cancer in man. (R. C. Kolosseus.) *Minn. Med.* 1975, **58**, 232.

On the immunity in patients with bladder cancer. (Ph de Boisgisson *et al.*) *Ann. Urol.* 1975, **9**, 21.

Failure of ascorbic acid to inhibit FANFT-induced bladder cancer. (M. S. Soloway *et al.*) *J. Urol.* 1975, **113**, 483.

Lactic dehydrogenase isoenzymes in human bladder cancer. (H. C. Bredin *et al.*) *J. Urol.* 1975, **113**, 487.

Recurrence prevention of bladder papilloma with triethylenthiophosphoradmide (thiotepa). (B. Riedel *et al.*) *Urologe*, 1975, **14**, 87.

Malignant pheochromocytoma of bladder: late development of renal cell carcinoma. (D. P. DeKlerk *et al.*) *J. Urol.* 1975, **113**, 864.

Experimental Investigations. Experimental studies on the sympathetic inhibition in the guinea pig bladder. (S. Yoda.) *Jap. J. Urol.* 1975, **66**, 140.

A recanning electron microscopic study on the urotheliums. 1. Ultrastructure of the urothelial surface of the bladder. (I. Kumagai.) *Jap. J. Urol.* 1975, **66**, 131.

An ultrastructure study of the urinary bladder in children correlated with histological bacteriological and clinical findings. (M. Haynes *et al.*) *J. Clin. Path.* 1975, **28**, 176.

Monolayer culture of normal rat bladder mucosal epithelium. (T. Ikeuchi.) *Jap. J. Urol.* 1975, **66**, 149.

Systematic use of suprapubic bladder puncture for voiding cysto-urethrography in infants and children. (D. Claus.) *Ann. Radiol.* 1975, **18**, 331.

An experimental pathological study of the regenerative activity on the mucosal epithelium of the urinary bladder—with special reference to the autoradiographic and electron microscopic observations. (Y. Hiraoka.) *Jap. J. Urol.* 1975, **66**, 303.

Mechanical Disorders *see* **Micturition.**

Operative Procedures. One-stage reconstruction for exstrophy of the bladder in girls. (D. W. Furnas *et al.*) *Plast. Reconstr. Surg.* 1975, **56**, 61.

Clinical studies on cystoplasty. A study on cystoplasty by regeneration of contracted bladder using novectane (liquid synthetic resin)-sprayed thin. (J. Taguchi and K. Saito.) *Jap. J. Urol.* 1975, **66**, 239.

Supplementary reconstruction of the urinary bladder with biodegradable material. (T. Agishi *et al.*) *Jap. J. Urol.* 1975, **66**, 263.

Effect of suture materials on healing wounds of bladder (J. C. Hastings *et al.*) *Surg. Gynec. Obstet.* 1975, **140**, 933.

Trocar-catheter for suprapubic cystostomy. (G. Frolich and R. Engelking.) *Urologe*, 1975, **14**, 150.

Cardiac rhythm in men during cystoscopy. (H. M. Kimbrough *et al.*) *J. Urol.* 1975, **113**, 846.

Contracted bladder and ureteral diversion—one approach to reconstruction. (A. D. Perlmutter *et al.*) *J. Urol.* 1975, **113**, 716.

Continent rectal bladder using intrasphincteric pull-through (a contribution to treatment of exstrophied bladder). (C. Janneck.) *Z. KinderChir.* 1975, **16**, 180.

PROSTATE

Infections and Prostatitis. Search for uro-genital tract infections in patients with symptoms of prostatitis. Studies on aerobic and strictly anaerobic bacteria, mycoplasmas, fungi, trichomonads and viruses. (P. A. Mårdh and S. Colleen.) *Scand. J. Urol. Nephrol.* 1975, **9**, 8.

Relationship between orificial insufficiency of prostatic ducts and urinary infection in infancy and childhood. (G. Theander.) *Ann Radiol.* 1975, **18**, 507.

Usefulness of prostatic massage. (R. H. Chase.) *Patient Care*, 1975, **9**, 105.

The concentration of sulphamethoxazole and trimethoprim in human prostate gland. (W. Oosterlinck *et al.*) *Brit. J. Urol.* 1975, **47**, 301.

Mycoplasma prostatourethritis. (F. J. Marx and A. Hofstetter.) *Münch. Med. Wschr.* 1975, **117**, 1023.

Plasma zinc levels in prostatic disease. (E. G. Willden and M. R. G. Robinson.) *Brit. J. Urol.* 1975, **47**, 295.

The proliferation of prostatic epithelium in chronic prostatitis. (R. Stiens *et al.*) *Urol. Res.* 1975, **3**, 21.

Electric pulsed current therapy of chronic prostatitis. (T. V. Surkov *et al.*) *Sovet. Med.* 1975, Apr. no. 4, 151.

Nonspecific inflammatory lesions of the prostate: spectrum and patterns. (E. B. Attah.) *Int. Surg.* 1975, **60**, 158.

Benign Prostatic Hypertrophy. Medrogestone: prospective study in pharmaceutical management of benign prostatic hyperplasia. (D. F. Paulson and R. D. Kane.) *J. Urol.* 1975, **113**, 811.

Testosterone and oestradiol-17β production rates in a patient suffering from hypertrophy of the prostate. (F. Bayard *et al.*) *Ann. Endocr.* 1975, **35**, 563.

A systematic study of testosterone metabolism in benign prostatic hypertrophy (BPH): in vitro results. (J. E. Altwein and F. Orestano.) *Urol. Res.* 1975, **2**, 143.

Morphological responses of benign human prostatic hypertrophic tissue to chemotherapeutic agents in an in vitro culture system. (M. J. Varkarakis *et al.*) *J. Med.* 1975, **6**, 65.

Carcinoma. Neoplastic perineal implantation following needle biopsy. (A. Puigvert.) *Urol. Int.* 1975, **30**, 305.

Epidemiologic characteristics of patients with prostatic neoplasms. (H. K. Armenian *et al.*) *Amer. J. Epidem.* 1975, **102**, 47.

Early diagnosis of prostatic carcinoma. (D. Volter and H. Ziegler.) *Deutsch. Med. Wschr.* 1975, **100**, 1573.

Cytological examination for determining the therapeutic response of prostatic carcinoma to hormonal therapy. (A. Rost *et al.*) *Urol. Int.* 1975, **30**, 245.

Etiologic factors in carcinoma of the prostate. (R. M. Mulligan.) *Ann. Clin. Lab. Sci.* 1975, **5**, 82.

Experiences with iliac crest biopsy by carcinoma of prostate. (M. W. Kollermann *et al.*) *Urologe*, 1975, **14**, 57.

Plasmocytoma—false diagnosis dedifferentiated carcinoma of prostate. (K. J. Peters and G. Ludwig.) *Urologe*, 1975, **14**, 92.

Radical perineal prostatectomy with bilateral orchiectomy for carcinoma of prostate. (J. Williams *et al.*) *J. Urol.* 1975, **113**, 380.

Clinical experience with supervoltage radiotherapy in carcinoma of prostate: preliminary report. (J. S. Mollenkamp *et al.*) *J. Urol.* 1975, **113**, 374.

Extended biopsy followup after full course radiation for resectable prostatic carcinoma. (R. A. Sewell *et al.*) *J. Urol.* 1975, **113**, 371.

Comparison between single and multiple drug therapy in treatment of carcinoma of prostate. (L. M. King *et al.*) *Penn. Med.* 1975, **78**, 61.

Treatment of carcinoma of the prostate. (J. Sans-Sabrafen.) *Med. Clin.* 1975, **64**, 319.

The role of lymphography in "apparently localised" prostatic carcinoma. (R. A. Castellino.) *Lymphology*, 1975, **8**, 16.

Occult transitional cell carcinoma of prostate presenting as skin metastasis. (M. Razvi *et al.*) *J. Urol.* 1975, **113**, 734.

Squamous carcinoma of the prostate. (G. F. Gray *et al.*) *J. Urol.* 1975, **113**, 736.

Evaluation of lymphangiography in staging carcinoma of prostate. (J. C. Cerny *et al.*) *J. Urol.* 1975, **113**, 367.

Coagulation disorders in prostatic carcinoma. (F. J. Marx *et al.*) *Urologe*, 1975, **14**, 127.

Morphology of clinical stage 0 of prostatic carcinoma (incidental carcinoma). (G. Dhom and B. Hautumann.) *Urologe*, 1975, **14**, 105.

Therapy of carcinoma of the prostate and case control (ii). (C. E. Alken *et al.*) *Urologe*, 1975, **14**, 111.

Inhibition of platelet aggregation under estrogen-treatment in patients with carcinoma of prostate. (M. Eisen *et al.*) *Urologe*, 1975, **14**, 132.

Megestrol acetate for treatment of advanced carcinoma of the prostate. (D. E. Johnson *et al.*) *J. Surg. Oncol.* 1975, **7**, 9.

Osteomalacia and carcinoma of prostate with major redistribution of skeletal calcium. (D. J. Hosking *et al.*) *Brit. J. Radiol.* 1975, **48**, 451.

Precautionary examination on carcinoma of the prostate gland in the district of Worbis. (G. Raasch *et al.*) *Deutsch. Gesundh.* 1974, **30**, 1116.

Bone scanning in patients with carcinoma of the prostate and bone metastases. (E. Dienstl *et al.*) *Wien. Med. Wschr.* 1975, **125**, 388.

Effect of long-term estrogen treatment on liver function in patients with prostatic carcinoma. (T. Ishibe.) *J. Urol.* 1975, **113**, 829.

Clinical management of carcinoma of the prostate associated with bilateral ureteral obstruction. (A. U. Khan and D. C. Utz.) *J. Urol.* 1975, **113**, 816.

Studies on etiology of prostatic cancer. Editorial *West Virginia Med. J.* 1975, **71**, 186.

Carcinoma of the prostate. (K. J. Rossman and W. W. Bohnert.) *Arizona Med.* 1975, **32**, 484.

Serial fluorine-18 bone scans in the follow-up of carcinoma of the prostate. (A. C. Buck *et al.*) *Brit. J. Urol.* 1975, **47**, 287.

Oestrogen therapy and serum cortisol in carcinoma of the prostate. (A. Morales *et al.*) *Brit. J. Urol.* 1975, **47**, 283.

Immunologic alterations in patients with prostatic carcinoma. (S. Brosman *et al.*) *J. Urol.* 1975, **113**, 841.

Benign killer: carcinoma of the prostate. (D. J. Krauss and O. M. Lilien.) *J. Urol.* 1975, **113**, 820.

Choice of therapy for prostatic cancer. (V. F. Marshall.) *J. Urol.* 1975, **113**, 285.

Effect of hormonal therapy on plasma FSH, LH and testosterone levels in prostatic cancer. (M. Shirai *et al.*) *Jap. J. Urol.* 1975, **66**, 59.

The screening of prostatic cancer. (C. Bollack.) *J. Med. Strasbourg*, 1975, **6**, 97.

Telecobalt therapy for prostatic cancer: rationale, results and future considerations. (M. McLoughlin *et al.*) *J. Urol.* 1975, **113**, 378.

Metastatic bone diseases with osteomalacia during prostatic cancer. Two cases. (F. Delbarre *et al.*) *Nouv. Presse Méd.* 1975, **4**, 1277.

Prostatic fluid lactic dehydrogenase isoenzyme patterns of prostatic cancer and hyperplasia. (R. C. Hein *et al.*) *J. Urol.* 1975, **113**, 511.

Correlation of pre-treatment serum 17-hydroxycorticosteroid values with survival in patients with prostatic cancer. (C. E. Blackard *et al.*) *J. Urol.* 1975, **113**, 517.

Migration-inhibitory effect of serum from patients with prostatic cancer. (R. J. Ablin *et al.*) *Oncology*, 1974, **30**, 423.

Serum lipid levels and thromboembolic complications during estrogen therapy of prostatic cancer. (E. A. Sotaniemi and M. J. Kontturi.) *Scand. J. Urol. Nephrol.* 1975, **9**, 89.

Assessment of results following endocrine therapy for prostatic cancer. (H. W. G. Baker *et al.*) *J. Urol.* 1975, **113**, 824.

Prostatic cancer and SCH-13521: 11. Histological alterations and pituitary gonadal axis. (G. R. Prout *et al.*) *J. Urol.* 1975, **113**, 834.

Leiomyosarcoma of the prostate. An autopsy case. (K. Fujita.) *Jap. J. Urol.* 1975, **66**, 106.

Transurethral electroresection of prostatic adenoma. (E. Hertel.) *München. Med. Wschr.* 1975, **117**, 813.

105 prostatic adenomectomies with continuous trans-vesical aspiration using a Saratoga catheter. (R. Luzuy *et al.*) *Chirurgie*, 1975, **101**, 396.

Role of radiation therapy in definitive treatment of adenocarcinoma of prostate. (G. R. Ray and M. A. Bagshow.) *Ann. Rev. Med.* 1975, **26**, 567.

Physiology and Experimental Studies. Normal paraganglia in human prostate. (S. R. Freedman and R. L. Goldman.) *J. Urol.* 1975, **113**, 874.

Urethral pressure profile in prostatic surgery. (J. C. Djurhuus *et al.*) *Scand. J. Urol. Nephrol.* 1975, **9**, 87.

Adrenergic and cholinergic receptors in the human prostate, prostatic capsule and bladder neck. (M. Caine *et al.*) *Brit. J. Urol.* 1975, **47**, 193.

Ultrastructural characteristics of "aging" of human prostate cells in monolayer cell culture. (J. F. Riemann *et al.*) *Urol. Res.* 1975, **3**, 13.

Separation of cells with histochemically demonstrable acid phosphatase activity from suspensions of human prostatic cells in an isokinetic gradient of ficoll in tissue culture medium. (S. R. Helms *et al.*) *Amer. J. Path.* 1975, **80**, 79.

Testosterone and progesterone metabolism in the human prostate. (J. P. Bercovici *et al.*) *Ann. Endocr.* 1975, **36**, 111.

Relationship between urinary infection and orificial insufficiency of prostatic ducts in infancy and childhood. (G. Theander.) *Pediat. Radiol.* 1975, **3**, 158.

Investigatory Procedures. Radiozinc as a scintigraphic agent for human prostate. (J. Fruhling and A. Coune.) Reply (G. D. Chisholm). *J. Nucl. Med.* 1975, **16**, 495, 496.

Needle biopsy by a modified approach in prostatic diseases. (M. Ahmad *et al.*) *Int. Surg.* 1975, **60**, 164.

Operative Procedures. Diagnostic criteria for indication of total prostatectomy. (M. Marquardt and H. U. Grob.) *Helv. Chir. Acta*, 1975, **42**, 387.

Later complications following prostatectomy for adenoma. (V. Petronic and Z. Sumaracpetronic.) *Helv. Chir. Acta*, 1975, **42**, 347.

Traction of catheter for hemostasis following prostatectomy. (P. W. Boer and C. L. A. H. Bruijnen.) *Helv. Chir. Acta*, 1975, **42**, 353.

Suitable doses of coagulant on retropubic prostatectomy. (K. Ueda *et al.*) *Jap. J. Urol.* 1975, **66**, 363.

Unusual complications of prostatectomy. (J. Cibert.) *J. Urol. Néphrol.* 1975, **81**, 187.

Transurethral prostatic resection in patients with prosthetic cardiac valves. (J. Mulcahy *et al.*) *J. Urol.* 1975, **113**, 642.

Haemostatic (malament) suture in transvesical prostatectomy—preliminary report. (H. F. Given *et al.*) *Irish Med. J.* 1975, **68**, 199.

The effect of dicynene on blood loss during and after transurethral resection of the prostate. (J. M. Symes *et al.*) *Brit. J. Urol.* 1975, **47**, 203.

Test yourself: a case study of the transurethral resection of the prostate gland. (J. Testa.) *Amer. Assoc. Nurs. Anesth.* 1975, **43**, 164.

Urinary incontinence following total prostatovesiculectomy. (K. Haubensak.) *Urologe*, 1975, **14**, 53.

Is urography necessary for patients with acute retention of urine before prostatectomy? (V. Marshall *et al.*) *Brit. J. Urol.* 1975, **47**, 73.

100 prostatectomies sans cathéter urétral. (W. von Niederhäusern.) *Helv. Chir. Acta*, 1975, **42**, 65.

Early and late results after cryosurgical treatment of bladder neck obstructions. (H. J. Peters *et al.*) *Urologe*, 1975, **14**, 137.

Prevention of complications in transurethral electrosection of prostatic glands. (B. Honger and J. M. Baumann.) *Helv. Chir. Acta*, 1975, **42**, 391.

New concept on the T.U.R. prostate syndrome. (J. J. Iglésias *et al.*) *J. Urol. Néphrol.* 1975, **81**, 191.

The distribution and retention of cadmium 115m in the rat following injection into the prostate. (E. Aughey *et al.*) *Brit. J. Urol.* 1975, **47**, 185.

URETHRA

Congenital Anomalies. The development of obstruction in true valves and in functionally valve-like abnormalities of the male posterior urethra. (H. G. Ringertz and O. Eklof.) *Ann. Radiol.* 1975, **18**, 507.

Incomplete duplication of the urethra with intrarectal opening of the posterior channel. (J. P. Desgrez and J. Cendron.) *J. Urol. Néphrol.* 1975, **81**, 169.

Supernumerary urethra in boys (about 12 personal observations). (J. Cendron and J. P. Desgrez.) *J. Urol. Néphrol.* 1975, **81**, 157.

Double and bifid urethras. (C. Chatelain *et al.*) *Ann. Chir. Infant.* 1975, **16**, 75.

Anterior transposition of urethra. (C. C. Winter and V. Braren.) *J. Urol.* 1975, **113**, 491.

Psychological factors in hypospadias repair. (M. Robertson and D. Walker.) *J. Urol.* 1975, **113**, 698.

Indication, techniques and results of operative correction of hypospadias using modification of original Denis Browne technique. (H. Marberger and A. Decristofore.) *Urologe*, 1975, **14**, 117.

Meatal advancement for distal hypospadias without chordee. (A. D. Perlmutter and A. D. Vatz.) *J. Urol.* 1975, **113**, 850.

A long-term review of hypospadias surgery [summary]. (B. C. Sommerlad.) *Proc. Roy. Soc. Med.* 1975, **68**, 402.

Study of the anterior urethra in hypospadias cases by means of silicone rubber casts. (P. L. G. Townsend.) *Proc. Roy. Soc. Med.* 1975, **68**, 403.

Gynecomastia and hypospadias in a fertile patient. (F. J. Gómez-Pérez *et al.*) *Rev. Invest. Clin.* 1975, **27**, 81.

Experience with the Denis Browne repair of hypospadias. (J. H. Goldin.) *Proc. Roy. Soc. Med.* 1975, **68**, 401.

Epispadias. (D. I. Williams.) *Proc. Roy. Soc. Med.* 1975, **68**, 399.

Trauma. Management of complete disruption of the posterior urethra. (R. A. Janknegt.) *Brit. J. Urol.* 1975, **47**, 305.

Pediatric urethral and perineal injuries. (R. A. Garrett.) *Pediat. Clin. N. Amer.* 1975, **22**, 401.

Infections and Urethral Syndrome. The use of polymixin B as a urethral lubricant to reduce the post-instrumental incidence of bacteriuria in females. An exploratory study. (K. H. Chavigny.) *Int. J. Nurs. Stud.* 1975, **12**, 33.

Occurrence of mycoplasma in the urethra of healthy men. (H. Blenk *et al.*) *Münch. Med. Wschr.* 1975, **117**, 1029.

Minocycline in the treatment of non-gonococcal urethritis. (R. R. Willcox *et al.*) *Brit. J. Vener. Dis.* 1975, **51**, 206.

Non-specific urethritis and the tetracyclines. (A. S. Grimble and K. L. Amarasuriya.) *Brit. J. Vener. Dis.* 1975, **51**, 198.

Nevigramon in therapy of non-gonorrheal urethritis in men. (A. I. Lopatin.) *Vestn. Derm. Vener.* 1975, Feb., 71.

Chronic non-specific urethritis—urethral irrigation with hydrocortisone (a preliminary report). (A. O. Aina.) *Nigerian Med. J.* 1975, **5**, 30.

Non-specific urethritis in Nigerians. A clinical trial of vibramycin (Doxycycline). (A. O. Osoba.) *Nigerian Med. J.* 1975, **5**, 26.

Microorganisms observed in 80 cases of acute urethritis and their sensitivity to various antibiotics. (G. Mezzadra *et al.*) *G. Ital. Derm.* 1975, **110**, 57.

Stricture. Urethral stenosis due to non-specific urethritis. (E. Schrameck *et al.*) *J. Urol. Néphrol.* 1975, **81**, 239.

Treatment of posterior urethral stenosis by endoscopic resection. (P. Guillemin *et al.*) *J. Urol. Néphrol.* 1975, **81**, 208.

Operative techniques for perineal urethral stricture. (J. M. Baumann.) *Helv. Chir. Acta*, 1975, **42**, 337.

Anterior urethral diverticulum in the male—report of two cases. (B. Tanenbaum and M. E. Klinger.) *J. Amer. Geriat. Soc.* 1975, **23**, 234.

Diverticulum of the urethra in women, with 5 case reports. (A. Suhler and J. C. Masson.) *Ann. Urol.* 1975, **9**, 25.

Internal urethrotomy of urethral strictures in men under endoscopic control. (E. Matouschek and W. E. Michealis.) *Urol. Int.* 1975, **30**, 266.

Neoplasms. Primary cancer of the male urethra in Ibadan. (T. A. Junaid and E. O. Nkposong.) *Ghana Med. J.* 1974, **13**, 211.

Urethral metastasis from a presumed primary malignant melanoma presenting as postmenopausal bleeding. (J. F. B. Clarke.) *Proc. Roy. Soc. Med.* 1975, **68**, 227.

Investigatory Procedures. A new technique for urethrography. (R. L. Boltuch and A. F. Lalli.) *Radiology*, 1975, **115**, 736.

Clinic and diagnosis of sub-vesicular urethral disturbances. (O. A. Festge *et al.*) *Zbl. Chir.* 1975, **100**, 487.

Infusion urethrography in male patients. (H. Bartels and F. D. Hildebrand.) *Helv. Chir. Acta*, 1975, **42**, 343.

Operative Procedures. Results of internal urethrotomy under endoscopic control. (W. E. Michaelis and E. Matouschek.) *Helv. Chir. Acta*, 1975, **42**, 331.

Surgery on urethra masculina. (K. Bandhauer.) *Helv. Chir. Acta*, 1975, **42**, 321.

Results of internal urethrotomy for distal urethral stenosis in adults. (R. Harzmann and R. Chiari.) *Aktuel Urol.* 1975, **6**, 107.

Modification of the Foley catheter for use in a perineal urethrostomy. (D. E. Tolhurst.) *Plast. Reconstr. Surg.* 1975, **55**, 503.

The technique of results of one-stage island patch urethroplasty. (J. P. Blandy and M. Singh.) *Brit. J. Urol.* 1975, **47**, 83.

MICTURITION

General. Micturition troubles following abdomino-peritoneal amputations of the rectum for cancer. (A. Steg and L. Boccon-Gibbod.) *Ann. Urol.* 1975, **9**, 41.

Urinary prosthetic sphincter. (A. Middleton.) *Rocky Mountain Med. J.* 1975, **72**, 160.

Physiology. Effects of levodopa on bladder outlet. (M. I. Murdock *et al.*) *J. Urol.* 1975, **113**, 803.

A new urethroanal reflex revealed by sphincter electromyography. (A. P. Ruskin and J. E. Davis.) *Arch. Phys. Med.* 1975, **56**, 218.

Experimental studies on animals on bladder function following sacral blockade with alcohol. (D. Fischer *et al.*) *Anaesthesist*, 1975, **24**, 120.

Recovery of bladder function after spinal cord transection. (U. Jonas *et al.*) *J. Urol.* 1975, **113**, 626.

Complete external sphincterotomy: correlation between endoscopic observation and anatomic sphincter. (D. G. Linker and E. A. Tanagho.) *J. Urol.* 1975, **113**, 348.

A critical review of the management of bladder neoplasia using a modified form of Helmstein's pressure therapy. (R. W. Glashan.) *Brit. J. Urol.* 1975, **47**, 57.

Investigatory Procedures. Clinical applications of new uroflowmeter. (S. Raz and D. Adler.) *J. Urol.* 1975, **113**, 678.

Urethral profile: study of a technique. (J. L. Rottembourg *et al.*) *J. Urol. Néphrol.* 1975, **81**, 391.

A study of the bladder flow during distension in rabbits. (M. Dunn.) *Brit. J. Urol.* 1975, **47**, 67.

Local Disorders. Y-V cystoplasty for urinary retention following gynecologic surgery. (D. S. Dahl.) *Obstet. Gynec.* 1975, **46**, 109.

Intraspinal epidermoid tumor of sacral canal presenting with urinary retention. (W. Tipton *et al.*) *J. Urol.* 1975, **113**, 880.

Rétention aiguë d'urines. (M. le Guillou.) *Rev. Prat.* 1975, **25**, 2697.

Habituation and urinary retention. (J. L. Jammes *et al.*) *J.A.M.A.* 1975, **232**, 1264.

Bladder retention as a manifestation of a persisting constipation. (Ch. Bouffioux and J. de Leval.) *Acta Urol. Belg.* 1975, **43**, 77.

Urinary retention and intestinal obstruction associated with ano-rectal herpes simplex virus infection. (D. Goldmeier *et al.*) *Brit. Med. J.* 1975, **2**, 425.

Neurogenic Disorders. Urodynamic observations following spinal trauma. (D. G. Thomas *et al.*) *Brit. J. Urol.* 1975, **47**, 161.

The urological treatment of paraplegic patients at home. (R. Ascoli.) *Paraplegia,* 1975, **12**, 260.

Clinical application of electronic bladder stimulation in paraplegics. (J. H. Grimes *et al.*) *J. Urol.* 1975, **113**, 338.

Surgical reduction of bladder capacity in treatment for neurogenic bladder. (G. Arvis.) *Helv. Chir. Acta,* 1975, **42**, 411.

The treatment of infra-vesical obstructions of neurological bladders, 27 cases. (P. Mollard *et al.*) *J. Urol. Néphrol.* 1975, **81**, 349.

Urinary manometry in patients with spinal cord injury: neurological considerations in the rehabilitation of acute and chronic neurogenic bladder. (A. E. Rossier *et al.*) *Arch. Phys. Med.* 1975, **56**, 187.

Selective sacral rootlet rhizotomy for hypertonic neurogenic bladder. (S. K. Toczek *et al.*) *J. Neurosurg.* 1975, **42**, 567.

Urine flow measurement in diagnosis of neurogenic bladder dysfunction. (E. Schneider.) *Nervenarzt,* 1975, **46**, 203.

Electrostimulation of the neuropathic bladder. (J. Denes and J. Leb.) *J. Pediat. Surg.* 1975, **10**, 245.

Intermittent catheterization in neurogenic bladder dysfunction. (H. W. Herr.) *J. Urol.* 1975, **113**, 477.

Late effects of neurogenic bladder dysfunctions in paraplegics. (P. Hass and A. Terbizan.) *Urol. Int.* 1975, **30**, 181.

Incontinence Treatment. Stages of vegetative afferentation in reorganization of bladder control during intravesical electrotherapy. (F. Katona.) *Urol. Int.* 1975, **30**, 192.

Clinical experience with mentor bladder stimulator. 111 Patients with urinary vesical hypotonia. (D. C. Merrill.) *J. Urol.* 1975, **113**, 335.

Electronic stimulation of the human bladder: 9 years later. (D. B. Halverstadt and W. L. Parry.) *J. Urol.* 1975, **113**, 341.

Determination of incontinence using position cystography and urethrometry. (J. M. Baumann.) *Helv. Chir. Acta,* 1975, **42**, 379.

Colpocystography in cases of genital prolapse and urinary stress incontinence in women. (M. Lazarevski *et al.*) *Amer. J. Obstet. Gynec.* 1975, **122**, 704.

Urge incontinence in women. (A. Ingelman-Sundberg.) *Acta Obstet. Gynec. Scand.* 1975, **54**, 153.

Urinary stress incontinence and prolapse: assessment of colpocystography. (J. C. Brismontier.) *Ouest Med.* 1975, **28**, 785.

Urinary stress incontinence—differential diagnosis, pathophysiology and management. (T. H. Green.) *Amer. J. Obstet. Gynec.* 1975, **122**, 368.

First experiences with incontinence operation Kaufman iii (implantation of a silicongel prosthesis covered with polyurethanfoam). (B. Riedel *et al.*) *Urologe,* 1975, **14**, 121.

Repeat Marshall-Marchetti procedure for recurrent stress urinary incontinence. (R. A. Lee and R. E. Symmonds.) *Amer. J. Obstet. Gynec.* 1975, **122**, 219.

Incontinence des urines. (J. Aubert.) *Rev. Prat.* 1975, **25**, 2404.

Affective and urinary incontinence. (G. Harrer.) *Wien. Med. Wschr.* 1975, **125**, 341.

Anterior urethropexy according to Lapides in stress urinary incontinence. A follow-up study. (T. Sundin and S. Pettersson.) *Scand. J. Urol. Nephrol.* 1975, **9**, 28.

Free fascial sling to correct urinary incontinence after prostatic surgery. Results of eight operated patients. (S. Pettersson.) *Scand. J. Urol. Nephrol.* 1975, **9**, 24.

Severe incontinence of urine-11 and its surgical treatment (indications for typical operations in cases of incontinence of urine and their results). (E. Hochuli *et al.*) *Geburtsh. Frauenheilk.* 1975, **35**, 181.

Free autogenous muscle transplantation in two cases of total anal incontinence. (L. Hakelius.) *Acta Chir. Scand.* 1975, **141**, 69.

Enuresis. An historical account of nocturnal enuresis and its treatment. (M. A. Salmon.) *Proc. Roy. Soc. Med.* 1975, **68**, 443.

Flavoxate hydrochloride in the treatment of childhood enuresis. (V. J. Gururaj *et al.*) *Clin. Med.* 1975, **82**, 25.

Dialogue à propos de conduite à tenir devant une énurésie de l'enfant. (D. J. Duché.) *Rev. Prat.* 1975, **25**, 2406.

Vaginal reflux, a cause of enuresis? (J. Queloz *et al.*) *Praxis,* 1975, **64**, 589.

Enuresis: organic or psychosomatic disorder? (D. T. Mahony and A. R. Kendall.) *J.A.M.A.* 1975, **232**, 548.

Conduite à tenir devant une énurésie de l'enfant. (D. J. Duché.) *Rev. Prat.* 1975, **25**, 1374.

The use of self-hypnosis in the treatment of childhood nocturnal enuresis. A report on forty patients. (K. Olness.) *Clin. Pediat.* 1975, **14**, 273.

URINARY DIVERSION

Whole body potassium in patients with uterosigmoid anastomoses. (K. Boddy *et al.*) *Brit. J. Urol.* 1975, **47**, 277.

Bladder substitution with continent ileum pouch. Experimental study on dogs. (A. Sulmoni *et al.*) *Urol. Int.* 1975, **30**, 273.

Colonic neoplasma complicating ureterosigmoidostomy. (A. Lasser and A. E. Acosta.) *Cancer,* 1975, **35**, 1218.

Jejunal conduits: technique and complications. (M. Golimbu and P. Morales.) *J. Urol.* 1975, **113**, 787.

Colonic neoplasms following ureterosigmoidostomy. (J. Y. Rivard *et al.*) *J. Urol.* 1975, **113**, 781.

Ureterosigmoidostomy: critical review of 173 cases. (H. Zincke and J. W. Segura.) *J. Urol.* 1975, **113**, 324.

Relative diverticula of ileal conduit. (J. F. Redman and N. K. Bissada.) *J. Urol.* 1975, **113**, 568.

Supravesicular urinary derivation from gynecological indications. (E. Michalowski and M. Galka.) *Z. Gynäk.* 1975, **97**, 321.

Studies on the urinary tract substitution: long-term observations on 107 cases of colocystoplasty. (T. Omoto.) *Jap. J. Urol.* 1975, **66**, 341.

Indications for urinary diversion in children. (E. Pakarovic.) *Z. KinderChir.* 1975, **16**, 167.

Late results of ileo-cystoplasty. (L. Durand *et al.*) *J. Urol. Néphrol.* 1975, **81**, 1.

Urinary diversion: the physiological rationale for non-refluxing colonic conduits. (J. P. Richie and D. G. Skinner.) *Brit. J. Urol.* 1975, **47**, 269.

Urinary diversion: rectal bladder combined with intrasphincteric perineal colostomy. 3. Clinical study on the postoperative acute pyelonephritis. (M. Matsuda *et al.*) *Jap. J. Urol.* 1975, **66**, 254.

Nonrefluxing colon conduit for temporary or permanent urinary diversion in children. (W. H. Hendren.) *J. Pediat. Surg.* 1975, **10**, 381.

Palliative urinary diversion for pelvic malignancy. (E. N. Brin *et al.*) *J. Urol.* 1975, **113**, 619.

Isolated sigmoid segment: its value in temporary urinary diversion and reconstruction. (D. G. Skinner *et al.*) *J. Urol.* 1975, **113**, 614.

Intermittent catheterization rather than urinary diversion in children with meningomyelocele. (R. P. Lyon *et al.*) *J. Urol.* 1975, **113**, 409.

Colonic urinary diversion: 10 years of experience. (P. Morales and M. Golimbu.) *J. Urol.* 1975, **113**, 302.

Ileocecal conduit for temporary and permanent urinary diversion. (L. Zinman and J. A. Libertino.) *J. Urol.* 1975, **113**, 317.

Ileocecal bladder: new method for urinary diversion after radical cystectomy (preliminary report). (M. Khafagy *et al.*) *J. Urol.* 1975, **113**, 314.

Transverse colon conduit: preferred method of urinary diversion for radiation-treated pelvic malignancies. (J. D. Schmidt *et al.*) *J. Urol.* 1975, **113**, 308.

LITHIASIS (in general)

Urinary lithiasis and parathyroid adenoma. (J. M. Colas *et al.*) *J. Urol. Néphrol.* 1975, **81**, 419.

Experiences in region with high incidence of lithiasis. (F. Bianchi.) *Helv. Chir. Acta*, 1975, **42**, 403.

A special cause of urinary lithiasis: functional disorders of the terminal ileum. (Ph. Cassan and A. Baglin.) *Nouv. Presse Méd.* 1975, **4**, 1729.

Urinary lithiasis in children, 106 cases. (D. Beurton and J. Cukier.) *J. Urol. Néphrol.* 1975, **81**, 219.

Urolithiasis in Irish children. (P. Puriet *et al.*) *Irish Med. J.* 1975, **68**, 192.

Urinary lithiasis in childhood in the Bristol clinical area. (C. G. C. Gaches *et al.*) *Brit. J. Urol.* 1975, **47**, 109.

Some data on urinary stones which were passed. (D. J. Sutor and S. E. Wooley.) *Brit. J. Urol.* 1975, **47**, 131.

An observation on the composition and recurrence of urinary calculi. (E. Takasaki.) *Urol. Int.* 1975, **30**, 228.

Hypercalcemia and unilateral nephrocalcinosis. (H. H. Advani and G. S. Sidhu.) *J.A.M.A.* 1975, **232**, 161.

Excretion of inhibitors of calcification in urine. Part 1. Findings in control subjects and patients with renal stones. Part 2. Findings in patients with chronic renal failure. (D. G. Oreopoulos *et al.*) *Cand. Med. Ass. J.* 1975, **112**, 827, 832.

Electrohydraulic lithotripsy: experimental study and case reports with stone disintegrator. (A. M. Raney.) *J. Urol.* 1975, **113**, 345.

URINARY TRACT INFECTIONS

Quick office test for bacteriuria. *Patient Care*, 1975, **9**, 37.

Quantitative bacteriuria. Practical value of two "dip slides" tests. (H. Cloppet *et al.*) *Méd. Mal. Infect.* 1975, **5**, 243.

Bacteriuria in the catheterized patient. (P. Gonick *et al.*) *J.A.M.A.* 1975, **233**, 253.

Detection of bacteriuria by luciferase assay of adenosine triphosphate. (A. Thore *et al.*) *J. Clin. Microbiol.* 1975, **1**, 1.

Self-screening for significant bacteriuria. (C. M. Kunin and J. E. DeGroot.) *J.A.M.A.* 1975, **231**, 1349.

Screening for bacteriuria in newborns: experience with plastic bags. (G. G. Biasini *et al.*) *Helv. Paediat. Acta*, 1974, **29**, 575.

Urinary antiseptics in asymptomatic bacteriuria of pregnancy. (E. T. Furness *et al.*) *New Zeal. Med. J.* 1975, **81**, 417.

Screening methods for covert bacteriuria in schoolgirls. (B. Edwards *et al.*) *Brit. Med. J.* 1975, **2**, 463.

Asymptomatic bacteriuria in schoolgirls I, II, III. (U. Lindberg *et al.*) *Acta Paediat. Scand.* 1975, **64**, 425, 432, 437.

Asymptomatic bacteriuria in school girls IV. (U. Lindberg *et al.*) *Acta Paediat. Scand.* 1975, **64**, 574.

Cephradine in urinary tract infections—double blind comparison with ampicillin. (R. A. L. Low and T. K. Clarke.) *Curr. Med. Res.* 1975, **3**, 211.

Urinary tract problems in women are linked to sexual activity. (S. Kent.) *Geriatrics*, 1975, **30**, 145.

Informational basis for treatment of urinary tract infections. (G. Jackson.) *Infection*, 1975, **3**, 119.

Cefazolin—pharmacokinetics and clinical efficiency in urinary tract infections. (M. Franke and G. Manz.) *Med. Welt.* 1975, **26**, 1331.

Antimicrobial resistance in urinary tract infections. (T. E. Miller *et al.*) *New Zeal. Med. J.* 1975, **81**, 552.

Bacturcult in the diagnosis of urinary tract infection. (R. R. Bailey and E. Dann.) *New Zeal. Med. J.* 1975, **81**, 517.

Pathogenesis and management of urinary tract infections in women. (A. W. Asscher.) *Brit. J. Hosp. Med.* 1975, **12**, 546.

Coagulase-negative staphylococci and micrococci in urinary tract infections. (P. D. Meers *et al.*) *J. Clin. Path.* 1975, **28**, 270.

New developments in diagnosis and treatment of urinary tract infections. (C. M. Kunin.) *J. Urol.* 1975, **113**, 585.

Diagnosis, therapy and evaluation of successful treatment of chronic infections of urinary passages. (H. Pichler.) *Infection*, 1975, **3**, 57.

Bacteriological aspects on therapy of infections of urinary passages. (R. Gallien.) *Infection*, 1975, **3**, 56.

Recent observations on chronic non-obstructive urinary tract infection. (W. Brumfitt.) *Infection*, 1975, **3**, 53.

Controlled trial comparing co-trimoxazole and methenamine hippurate in the prevention of recurrent urinary tract infections. (S. Kalowski *et al.*) *Med. J. Aust.* 1975, **1**, 585.

Trimethroprim and sulfamethoxazole in urinary infections. (M. Alvo *et al.*) *Rev. Med. Chile*, 1975, **103**, 12.

Klebsiella urinary tract infection. (J. L. Faoagali.) *New Zeal. Med. J.* 1975, **81**, 286.

Infections of the urinary tract and prematurity. (H. J. Kümper.) *Fortschr. Med.* 1975, **93**, 537.

Recurrent urinary infections: causes and prevention. (G. Carroll) *Int. Urol. Nephrol.* 1975, **7**, 3.

Ampicillin, carbenicillin indanyl ester and nifuratel in the treatment of urinary infection in domiciliary practice. (B. I. Davies *et al.*) *Brit. J. Urol.* 1975, **47**, 335.

Drug therapy and prophylaxis of urinary tract infections in children—Podium discussion held at 71st Meeting of German Society for Pediatrics on September 11, 1974. Introduction. (H. Olbing.) *Mschr. Kinderheilk.* 1975, **123**, 518.

Duration of treatment for urinary tract infections in children. (J. M. Stansfield.) *Brit. Med. J.* 1975, **3**, 65.

TUMOURS (in General)

Urological manifestations of non-urological diseases (retroperitoneal tumors). (C. Dimopoulos *et al.*) *Acta Urol. Belg.* 1975, **43**, 90.

Tumors of the upper urothelium. (S. Rafla.) *Amer. J. Roentgen.* 1975, **123**, 540.

T. N. M. classification for urological tumours (U.I.C.C.)—1974. (D. M. Wallace *et al.*) *Brit. J. Urol.* **1975**, **47**, 1.

Phenacetin abuse and tumors of the urinary tract. (C. Landmannkolbert *et al.*) *Urologe*, 1975, **14**, 75.

The diagnostic and prognostic significance of delayed hypersensitivity skin testing in patients wih urological cancer. (G. Williams and J. E. Castro.) *Brit. J. Urol.* 1975, **47**, 97.

RADIOLOGY—ISOTOPE STUDIES—SONOGRAPHY

Urological indications of secondary radioionization. (R. Martinet.) *Helv. Chir. Acta*, 1975, **42**, 397.

Acute reactions to urographic contrast media. (P. Davies *et al.*) *Brit. Med. J.* 1975, **2**, 434.

Radiation therapy of keloids and hemangiomas. (A. Born and W. Born.) *München. Med. Wschr.* 1975, **117**, 907.

Radiology of suprarenal glands. (E. Voegeli and H. Kaser.) *Radiologie*, 1975, **15**, 149.

Radiation effects on rat testes. vii. Alterations in nucleic acids and P^{32} incorporation after partial body gamma-irradiation. (G. S. Gupta *et al.*) *Strahlentherapie*, 1975, **149**, 324.

The importance of radiological examination for the prognosis of obstructive renal changes. (R. V. Navarrete.) *München. Med. Wschr.* 1975, **117**, 547.

The place of ultrasound diagnosis in urology. (A. Kratochwil.) *Wien. Klin. Wschr.* 1975, **87**, 385.

SEMINAL VESICLE

Carcinoma of the seminal vesicle. (J. E. Lathem.) *Southern Med. J.* 1975, **68**, 473.

Transvesical approach to total seminal vesiculectomy. (V. A. Politano *et al.*) *J. Urol.* 1975, **113**, 385.

Antimicrobial activity of human seminal fluid. (P. A. Mårdh and S. Colleen.) *Scand. J. Urol. Nephrol.* 1975, **9**, 17.

VAS DEFERENS

General. Congenital absence of the vas deferens. (S. V. Rubin.) *Scand. J. Urol. Nephrol.* 1975, **9**, 94.

When and why does occlusion of the vas deferens affect the testis? (A. H. Horan.) *Fertil. Steril.* 1975, **26**, 317.

Uretero-vas deferens anastomosis associated with imperforate anus: an embryologically predictable occurrence. (J. A. Borger and A. B. Belman.) *J. Pediat. Surg.* 1975, **10**, 255.

Vasectomy. Vasectomy: informed consent. (A. J. Leader and S. D. Mumford.) *Texas Med.* 1975, **71**, 73.

The nitrofurans as sperm-immobilizing agents, their tissue toxicity and their clinical application in vasectomy. (P. S. Albert *et al.*) *Fertil. Steril.* 1975, **26**, 485.

Long-term effects of vasectomy on pituitary-gonadal function in man. (M. M. Varma *et al.*) *J. Clin. Endocr.* 1975, **40**, 868.

Plasma testosterone, luteinizing hormone and follicle-stimulating hormone after vasectomy. (R. E. Johnsonbaugh *et al.*) *Fertil. Steril.* 1975, **26**, 329.

Vasectomy in general practice. (N. S. Freeman.) *Practitioner*, 1975, **214**, 401.

Circulating antispermatozoa immunoglobulin G in men after vasectomy. (W. L. G. Quinlivan *et al.*) *Fertil. Steril.* 1975, **26**, 224.

Reconstruction of the Vas. Vas anastomosis: a return to simplicity. (S. S. Schmidt.) *Brit. J. Urol.* 1975, **47**, 309.

EPIDIDYMIS

Two cases of primary epididymal tumor. (H. Kuwatsuka *et al.*) *Jap. J. Urol.* 1975, **66**, 200.

Acute epididymitis attributable to chlamydial infection—preliminary report. (G. Heap.) *Med. J. Aust.* 1975, **1**, 718.

Biochemical changes in the spermatozoa and lumina contents of different regions of the epididymis of the rhesus monkey, *Macaca mulatta*. (R. Arora *et al.*) *Contraception*, 1975, **11**, 689.

Cellular proliferation and renewal in the various zones of the hamster epididymis after colchicine administration. (F. Nagy and R. H. Edmonds.) *Fertil. Steril.* 1975, **26**, 460.

The influence of ultra-high frequency electric field on spermatogenesis in treatment of patients with epididymitis. (Yu. I. Grachev and G. A. Voskresenskaya.) *Vestn. Derm. Vener.* 1975, Feb. 75.

Acute non-specific epididymitis—clinical analysis and therapy. (W. Weiss.) *Aktuel. Urol.* 1975, **6**, 95.

Acute non-specific epididymitis in boys. A survey based on 48 consecutive cases. (J. Gierup *et al.*) *Scand. J. Urol. Nephrol.* 1975, **9**, 5.

Brown patches in the epididymis (Plates XXXVIII and XXXIX). (M. J. Mitchinson *et al.*) *J. Path.* 1975, **115**, 57.

TESTIS

General. Radiation effects on testes VI. 5′ nucleotidase and adenosine triphosphatase following partial body gamma irradiation (English). *Radiobiol. Radiother.* 1975, **16**, 221.

Aberrant adrenal tissue: incidental finding during orchiopexy. (A. E. Feldman *et al.*) *J. Urol.* 1975, **113**, 706.

Selective scintigraphic lymphography of testis. (S. Spaventi *et al.*) *Radiol. Diagn.* 1974, **15**, 111.

Epidermoid cyst of the testicle. (F. Plaza *et al.*) *Int. Surg.* 1975, **60**, 231.

Comparative responses of isolated human testicular capsule to autonomic drugs. (C. F. Firlit *et al.*) *J. Urol.* 1975, **113**, 500.

Visceral lymphography of the testicles (English). (M. Kapnapos.) *Radiol. Diagn.* 1974, **15**, 315.

Congenital Anomalies. Dysplasia of the testis and epididymis. (G. Lingårdh *et al.*) *Scand. J. Urol. Nephrol.* 1975, **9**, 1.

Oxandrolone treatment of constitutional short stature in boys during adolescence—effect on linear growth, bone age, pubic hair and testicular development. (C. Martihenneberg *et al.*) *J. Pediat.* 1975, **86**, 783.

Bilateral anorchism. (J. M. Reckler *et al.*) *J. Urol.* 1975, **113**, 869.

Die chirurgische Sanierung der Hydrocele testis nach der Methode von Lord. (G. Mark and H. Stirnemann.) *Helv. Chir. Acta*, 1975, **42**, 61.

Maldescent. Staged orchiorrhaphy—therapeutic procedure in cryptorchic testicle with a short spermatic cord. (M. Zer *et al.*) *Arch. Surg.* 1975, **110**, 387.

Endocrine and morphological investigations in undescended testis. (H. Koch *et al.*) *Deutsch. Med. Wschr.* 1975, **100**, 683.

Determinations of micronucleus and analyses of chromosomes in the retentio testis. (C. Brock *et al.*) *Deutsch. Gesundh.* 1975, **30**, 991.

Differential treatment time for cryptorchidism. (L. Weissbach and B. Ibach.) *Deutsch. Med. Wschr.* 1975, **100**, 1030.

Optimal time for treating cryptorchidism. (G. Ludwig and J. Potempa.) *Deutsch. Med. Wschr.* 1975, **100**, 680.

Management of cryptorchid testis. (R. Baker.) *J.A.M.A.* 1975, **232**, 550.

Trauma and Torsion. So-called torsions of the hydatid cyst of Morgagni. (F. R. Banchieri *et al.*) *J. Urol. Néphrol.* 1975, **81**, 252.

Gangrene of testis as a complication in incarcerated inguinal hernia in infancy. (G. Menardi and H. Sauer.) *Z. KinderChir.* 1975, **16**, 421.

Torsion of the testis occurring on four occasions in two twin brothers. (L. Quénu and J. Picard.) *J. Urol. Néphrol.* 1975, **81**, 460.

Torsion of the testicle. (D. Meiraz *et al.*) *Harefuah*, 1975, **88**, 372.

Torsion of the testis in the newborn (A. W. Auldist and R. S. Ferguson.) *Aust. New. Zeal. J. Surg.* 1975, **45**, 14.

Neonatal testicular torsion in two brothers. (E. E. Castilla *et al.*) *J. Med. Genet.* 1975, **12**, 112.

Rupture of the testicle and epididymis. With ten case reports, three of which concern isolated rupture of the epididymis. (J. Hermabessière *et al.*) *Ann. Urol.* 1975, **9**, 35.

Infection. The testis in mice infected with *Mycobacterium leprae* (Plates L-LI). (R. J. W. Rees *et al.*) *J. Path.* 1975, **115**, 73.

Neoplasms. Malignant mesothelioma of the testicular tunica vaginalis. (J. Fishelovitch *et al.*) *Brit. J. Urol.* 1975, **47**, 208.

Leydigioma of the testis. (G. Lemaire *et al.*) *J. Urol. Néphrol.* 1975, **81**, 445.

A rare tumour of the testis (teratocarcinoma). (J. Boschi *et al.*) *J. Urol. Néphrol.* 1975, **81**, 266.

Androblastoma and germ cell tumor of same testis. (G. P. Trentini and B. Palmieri.) *J. Urol.* 1975, **113**, 725.

Clinical aspects and treatment of testicular tumors. (G. Staehler *et al.*) *München. Med. Wschr.* 1975, **117**, 777.

Retroperitoneal germ cell tumors with no apparent testicular involvement. (D. K. Montague.) *J. Urol.* 1975, **113**, 505.

Feminizing interstitial cell tumor of the testis: personal observations and a review of literature. (J. L. Gabrilove *et al.*) *Cancer*, 1975, **35**, 1184.

Germinal tumors of the testes. (H. Grabstald.) *C.A.* 1975, **25**, 82.

Vascular patterns of testicular tumors: microangiographic study. (S. Ichijo.) *J. Urol.* 1975, **113**, 360.

Testicular embryonary carcinoma: unique pulmonary metastasis controlled by ^{60}Co. (J. L. Genovés and R. Sancho.) *Radiologia*, 1975, **17**, 45.

Hemangiomas of the tunica albuginea testis. (N. W. Pfitzenmaier *et al.*) *Urol. Int.* 1975, **30**, 237.

Treatment of testicular cancer. (D. I. Twito and B. J. Kennedy.) *Ann. Rev. Med.* 1975, **26**, 235.

The treatment of low differentiated germinal cancers of the testis using mithramycin. (P. Ekman and L. E. Almgard.) *Scand. J. Urol. Nephrol.* 1975, **9**, 100.

Why are ovarian teratomas benign whilst teratomas of the testis are malignant? (T. J. Evans *et al.*) *Lancet*, 1975, **1**, 1360.

New chemotherapy (adriamycin, bleomycin and vincristin) of metastasizing malignant testicular teratoma. (S. Seeber *et al.*) *Deutsch. Med. Wschr.* 1975, **100**, 1319.

An experimental mouse testicular teratoma as a model for neuroepithelial neoplasia and differentiation 1. Light microscopic and tissue organ culture observations. (S. R. VandenBerg *et al.*) *Amer. J. Path.* 1975, **79**, 147.

PENIS

Cavernosogram study on valvular competence of human deep dorsal vein. (T. J. Fitzpatrick and J. F. Cooper.) *J. Urol.* 1975, **113**, 497.

Corpus cavernosum intercommunicating venous drainage system. (T. Fitzpatrick.) *J. Urol.* 1975, **113**, 494.

Scrotal skin resession phalloplasty. (R. B. Malkin *et al.*) *J. Urol.* 1975, **113**, 353.

Pagets disease of radix penis (nosological discussion). (G. Dubrulle *et al.*) *Bull Soc. Franc. Derm. Syph.* 1975, **82**, 63.

Penile burns due to application of roots. (D. J. Buchanan.) *Med. J. Zambia*, 1975, **9**, 42.

Solitary papular lesions on the penis in insufficiently treated early syphilis. A report of two cases. (A. Notowicz *et al.*) *Dermatologica*, 1975, **150**, 26.

Four V-flap repair of preputial stenosis (phimosis). (A. J. Emmett.) *Plast. Reconstr. Surg.* 1975, **55**, 687.

Giant condyloma acuminata (report of two cases). (M. M. Lal *et al.*) *Indian. J. Derm.* 1975, **20**, 51.

Devine's operation in the induratio penis plastica. (F. Bianchi.) *Acta Urol Belg.* 1975, **43**, 11.

Treatment of Peyronie's disease with procarbazine. (W. Oosterlinck and G. Renders.) *Brit. J. Urol.* 1975, **47**, 219.

Peyronie's disease. (J. Chesney.) *Brit. J. Urol.* 1975, **47**, 209.

Secondary closures of penile skin incisions. (C. E. Horton and C. J. Devine.) *Plast. Reconstr. Surg.* 1975, **55**, 630.

Three cases of congenital torsion of the penis. (H. Sugiura *et al.*) *Jap. J. Urol.* 1975, **66**, 160.

Hemangioma of penis with blue rubber-bleb nevus syndrome. (R. H. Smart and D. E. Newton.) *J. Urol.* 1975, **113**, 570.

Postcircumcision phimosis and its management. (J. F. Redman *et al.*) *Clin. Pediat.* 1975, **14**, 407.

A new operation for priapism. (J. Ebbehøj.) *Scand. J. Plast. Reconstr. Surg.* 1974, **8**, 241.

Priapism—pathogenesis and therapy. (R. Tscholl.) *Schweiz. Med. Wschr.* 1975, **105**, 517.

Micropenis associated with testicular agenesis. (D. B. Grant and M. J. Dillon.) *Arch. Dis. Child.* 1975, **50**, 247.

Treatment of penile plastic induration with radium moulages. (G. Alth and H. Koren.) *Strahlentherapie*, 1975, **149**, 262.

Penile cancer. (J. J. Doeven *et al.*) *Arch. Chir. Neerland.* 1975, **27**, 41.

Treatment of cancer of the penis with locoregional intra-arterial therapy. (A. Tarquini *et al.*) *Minerva Chir.* 1975, **30**, 817.

Kaposi's sarcoma of the penis. (W. Houston *et al.*) *Brit. J. Urol.* 1975, **47**, 315.

Leiomyosarcoma of penis—case report and review of the literature. (P. B. Hamal.) *Brit. J. Urol.* 1975, **47**, 319.

Fibrinolytic therapy in persistent priapism. Report of one case. (C. Cañizares *et al.*) *Sangre*, 1975, **20**, 207.

Sarcoidosis of the penis treated by radiotherapy. (M. Whittaker *et al.*) *Brit. J. Urol.* 1975, **47**, 325.

SCROTUM

Idiopathic fat necrosis in the scrotum. (R. Donohue and W. L. Utley.) *Brit. J. Urol.* 1975, **47**, 331.

Scrotal skin necrosis following snake bite. (S. N. Sinha.) *Brit. J. Urol.* 1975, **47**, 334.

Streptococcal cellulitis of scrotum and penis with secondary skin gangrene. (B. Haury *et al.*) *Surg. Gynec. Obstet.* 1975, **141**, 35.

A case of primary intrascrotal mucinous cystoadenocarcinoma. (H. Kuwatsuka *et al.*) *Jap. J. Urol.* 1975, **66**, 271.

Fournier's gangrene of the scrotum and penis, a case report. (H. O. DeBandi.) *J. Kentucky Med. Assoc.* 1975, **73**, 329.

On the diagnostics of the scrotal tumour. (K. M. Bauer.) *Med. Welt.* 1975, **26**, 1199.

Congenital transposition of the scrotum and penis. (J. E. Griffin and H. Hayes.) *Plast. Reconstr. Surg.* 1975, **55**, 710.

Pinol-aguade necrotic ulceration of the scrotum. (H. Perrot *et al.*) *Bull. Soc. Franc. Derm. Syph.* 1974, **81**, 645.

Fournier's syndrome: synergistic gangrene of the scrotum. (R. Rudolph *et al.*) *Amer. J. Surg.* 1975, **129**, 591.

Scrotal gangrene treated with oxygen under high pressure. (D. F. McDonald *et al.*) *J. Urol.* 1975, **113**, 364.

REPRODUCTION

Infertility. Sperm-agglutinating antibodies and testicular morphology in 59 men with azoospermia of cryptozoospermia. (J. Friberg and B. Kjessler.) *Amer. J. Obstet. Gynec.* 1975, **121**, 987.

Azoospermia due to occlusion—causes, diagnosis and possibilities for therapy—workshop on September 7, 1974 in Hamburg. (C. Schirren and D. Scholzjordan.) *Urologe*, 1975, **14**, 154.

Interest of pre-operative phlebography of the spermatic veins during surgery of varicocele. (R. Nataf and J. Leclère.) *J. Urol. Néphrol.* 1975, **81**, 226.

Valves of internal spermatic vein. (G. Ludwig *et al.*) *Aktuel. Urol.* 1975, **6**, 89.

The surgical aspects of male sterility. (M. Cognat.) *Lyon Chir.* 1975, **71**, 169.

(SEM/EDX): a tool of potential diagnostic value in cases of infertility. (K. G. Gould and D. E. Martin.) *J. Reprod. Med.* 1975, **14**, 197.

Cytogenetic studies of infertility. (H. Korner.) *Zbl. Gynak.* 1975, **97**, 467.

Present status of treatment of male factors of infertility in barren couples with special reference to cooperation between andrologists and gynaecologists. (C. Schirren.) *Geburts. Frauenhlk.* 1975, **35**, 334.

Testosterone rebound therapy in the treatment of male infertility. (H. Lamensdorf *et al.*) *Fertil. Steril.* 1975, **26**, 469.

Infertility practice and orthodox Jewish law. (J. A. Gordon *et al.*) *Fertil. Steril.* 1975, **26**, 480.

Varicocelectomy as therapy in male infertility: study of 504 cases. (L. Dubin and R. D. Amelar.) *J. Urol.* 1975, **113**, 640.

Infertility and semen non-liquefaction. (V. B. Wilson and R. G. Bunge.) *J. Urol.* 1975, **113**, 509.

Reproductive Physiology. Leydig cells, a report prepared for the Ford Foundation. (W. B. Neaves.) *Contraception*, 1975, **11**, 571.

Peripheral nerves controlling the closure of internal orifice during ejaculation. (Y. Kimura *et al.*) *Urol. Int.* 1975, **30**, 218.

Plasma LH and FSH response to LRH in boys with compensatory testicular hypertrophy. (Z. Laron *et al.*) *J. Clin. Endocr.* 1975, **40**, 977.

The semen of fertile men: statistical analysis of 1300 men. (N. E. Rehan *et al.*) *Fertil. Steril.* 1975, **26**, 492.

The intimate relationship between the urinary system and sexual function. (S. Kent.) *Geriatrics*, 1975, **30**, 138.

Disorders of ejaculation after surgery of the aortic bifurcation. (G. Lemaire *et al.*) *J. Urol. Néphrol.* 1975, **81**, 242.

Studies on the human testis. VI. NADH-linked reactions of microsomal steroid 20α- and 20β-hydroxysteroid dehydrogenase and 17α-hydroxylase. (H. Oshima *et al.*) *J. Clin. Endocr.* 1975, **40**, 426.

Testicular function in XYY men. (A. Baghdassarian *et al.*) *Johns Hopkins Med. J.* 1975, **136**, 15.

Secretions of testosterone and of oestradiol 17β by the human testis into plasma. The value of this study in cases of male sterility. (J. Salat *et al.*) *J. Gynéc. Obstét.* 1975, **4**, 217.

Male pseudohermaphroditism due to testicular 17β hydroxysteroid dehydrogenase deficiency. (G. Schaison and G. Dreyfus.) *Ann. Endocr.* 1975, **36**, 99.

Formation of 5α-dihydrotestosterone and other 5α-reduced metabolites from testosterone-^{14}C by human testicular tissues. (I. Takenaka *et al.*) *Yonago Acta Med.* 1974, **18**, 154.

Effect of human chorionic gonadotrophin on the dog seminiferous tubule, with and without experimental unilateral cryptorchism. (B. Ibach *et al.*) *Urol. Res.* 1975, **3**, 25.

Intersex. Problems of children with intersexual organ deformations. (L. Pelz.) *Zbl. Chir.* 1975, **100**, 495.

Surgical correction of ambiguous genitalia to female aspect. (M. Marberger *et al.*) *Aktuel. Urol.* 1975, **6**, 99.

Case of polyorchidism with intersex. (C. J. C. Renton.) *J. Urol.* 1975, **113**, 720.

Pregnancy and childbirth in a true hermaphrodite. (O. Narita *et al.*) *Obstet. Gynec.* 1975, **45**, 593.

Intersexuality and chromosomes. A case of male pseudohermaphroditism. (M. L. Oduori *et al.*) *East Afr. Med. J.*, 1975, **52**, 81.

Impotence. Studies on male sexual impotence. VIII Radiosotope penogram by means of ^{99m}Tc. (M. Shirai and M. Nakamura.) *Jap. J. Urol.* 1975, **66**, 183.

Unilateral gynecomastia and impotence during low dose spironolactone administration in men. (H. S. Zarren and P. McL. Black.) *Milit. Med.* 1975, **140**, 417.

Impotence as a practical problem. (J. Reckless and N. Geiger.) *DM*, 1975, May 3.

Diagnostic value of penile pulse pressure: Doppler study of impotence in diabetics. (D. Abelson.) *J. Urol.* 1975, **113**, 636.

Urologic counselling can overcome male sexual impotence. (P. S. Finkle and A. L. Finkle.) *Geriatrics*, 1975, **30**, 119.

Functional impotence treated by acupuncture. (M. I. Sergeev.) *Amer. J. Acupunct.* 1975, **3**, 67.

Treatment of organic impotence by implantation of silicone penile prosthesis. (S. Shishito *et al.*) *Urol. Int.* 1975, **30**, 211.

MISCELLANEOUS

Urogenital tuberculosis in 1974. (Ch. Viville.) *J. Chir.* 1975, **109**, 661.

Urologic complications in rectal surgery. (R. Winkler and G. A. Schlosser.) *Langenbecks Arch. Chir.* 1975, **338**, 235.

Metabolic changes in high-dose urography in babies. (H. W. Hayek *et al.*) *Ann. Radiol.* 1975, **18**, 325.

Use of continuous caudal anaesthesia in urological surgery. (C. Debras *et al.*) *Ann. Anesth. Franc.* 1974, **15**, Special no. 1, 123.

Urologic complications after operations for anorectal cancer, with an evaluation of preoperative intravenous pyelography. (J. Kramhøft *et al.*) *Dis. Colon Rectum*, 1975, **18**, 118.

Embolization in genitourinary disease. (R. Küss *et al.*) *Ann. Urol.* 1975, **9**, 1.

Non-urologic flank pain: diagnostic approach. (C. V. Hodges and J. M. Barry.) *J. Urol.* 1975, **113**, 644.

Blastomycosis of genitourinary tract. (H. U. Eickenberg *et al.*) *J. Urol.* 1975, **113**, 650.

Urological manifestations of non-urological diseases. (P. J. Wincqz.) *Acta Urol. Belg.* 1975, **43**, 71.

Urological manifestations of hematological diseases. (J. de Leval.) *Acta Urol. Belg.* 1975, **43**, 96.

Prevention of thrombo-embolic complications in urology sub-cutaneous calcium heparinate. (J. Aubert and P. Brisacier.) *J. Urol. Néphrol.* 1975, **81**, 175.

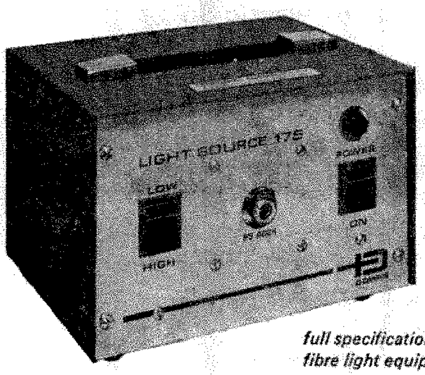
Chyluria. (U. Ko Ko *et al.*) *Int. Surg.* 1975, **26**, 237.

a choice of fibre light source for every situation

TYPE 2150

. . . for the theatre

Solid state for greatest reliability, with infinitely variable light output from two 150 watt quartz halogen lamps. A heat filter is incorporated to reduce cable temperature and increase cable life. Housed in a robust steel case, making a compact unit, the fan is quiet, and lamp changing is a simple matter.



TYPE 175

. . . for outpatient Departments

Using a 75 watt high efficiency quartz halogen lamp with di-chroic reflector, the Type 175 incorporates a High/low switch which gives increased lamp life at low settings. Of robust steel construction, the unit occupies very little space, and the fan is quiet in operation.

full specification and details of all fibre light equipment and instruments from

Downs Surgical Ltd

CHURCH PATH, MITCHAM, SURREY Tel 01-640 3422

UROLOGY

Edited by John Blandy M.A. D.M. M.Ch. F.R.C.S. 1976. 1344 pages, 807 illustrations. Two volumes, £46.00

This entirely new textbook of urology is aimed to meet the needs of the consultant in general surgery who wishes to keep up to date with recent advances and current thinking in urology, as well as the younger surgeon who intends to make urology his chosen speciality. Operative descriptions have been given where new advances have outstripped the orthodox textbooks of operative surgery but routine operations are, in general, omitted. Each chapter gives the scientific background of the subject to highlight the areas of uncertainty, and air those problems which form the topic of controversy among urologists today.

Contents
The urologist's armamentarium
The Kidney
Renal pelvis and ureter
The bladder
Prostate and urethra
Fistulae and diversion
The testicle
Adrenals

The Kidney: a Clinico-pathological Study
Priscilla Kincaid-Smith C.B.E. B.Sc. M.D. F.R.C.P. F.R.A.C.P. D.C.P. 1976. 464 pages, 376 illustrations. £18.50

Pathology of the Testis
Edited by R.C.B. Pugh M.D. F.R.C.Path. 1976. 504 pages, 264 illustrations. £18.50

Lecture Notes on Urology
John Blandy M.A. D.M. M.Ch. F.R.C.S. May 1976. 320 pages, 50 illustrations. Paper, about £3.75

Clinical Paediatric Nephrology
Edited by Ellin Lieberman M.D. May 1976. 568 pages, 252 illustrations. Lippincott, about £17.50

Urinalysis in Clinical Laboratory Practice
A.H. Free and Helen M. Free. 1976. 320 pages, CRC Press, £36.65

Blackwell Scientific Publications
Oxford London Edinburgh Melbourne

BRITISH JOURNAL OF PLASTIC SURGERY

Official Journal of the British Association of Plastic Surgeons

Edited by T. Gibson

Since its inception in 1948 the Journal has maintained a consistently high standard and remains one of the leading international journals in its field. It circulates to over 80 countries and about two-thirds of its original articles are by overseas authors. Not only does it inform surgeons in other countries of the pioneer work done in Britain but it serves as an international forum for the exchange of new ideas from all over the world.

Published quarterly in January, April, July and October. Volume 29, 1976.

Annual subscription	£10·00	USA $27.00
Single numbers	£ 3·00	USA $ 9.00

Subscriptions for USA should be sent to The Williams and Wilkins Company, 428 East Preston Street, Baltimore, Maryland, USA

Published under the E & S Livingstone imprint.

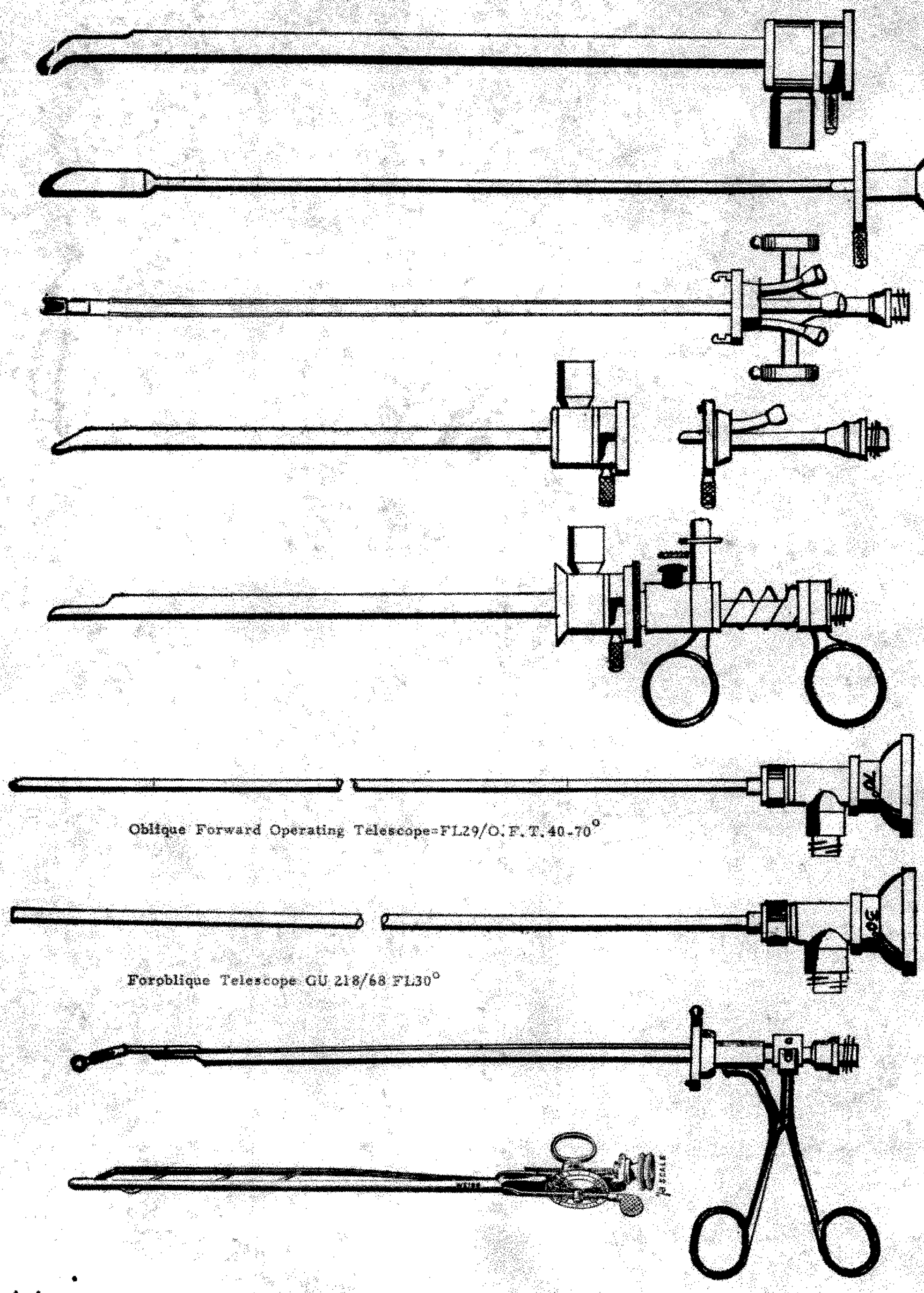
Subscription orders: Longman Group Ltd., Journals Division, 43/45 Annandale Street, Edinburgh EH7 4AT, Scotland.

All orders must be accompanied by the appropriate remittance.

Longman

Printed in Great Britain by T. & A. Constable Ltd., *Hopetoun Street, Edinburgh*

G.U. - BLANDY CYSTO-RESECTOSCOPE


Oblique Forward Operating Telescope=FL29/O.F.T.40-70°
Foroblique Telescope GU 218/68 FL30°

Made by
THE GENITO-URINARY MANUFACTURING CO. LTD.
28a 33–34 Devonshire Street London W1N 2AJ
Telephone:
01–935 2835/6/7
Telegrams:
Cystoscope London W1

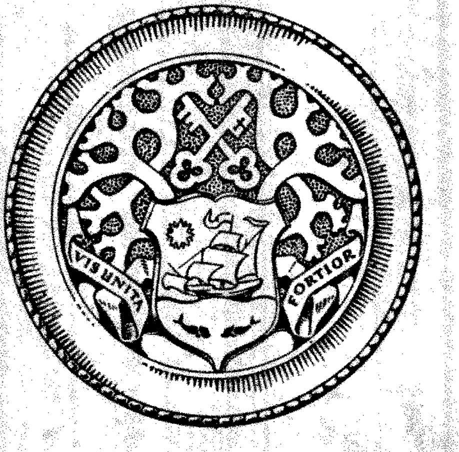
ISSN 0007-1331

5.11.76

Including
Abstracted Proceedings of the Urological Society of Australasia

BRITISH JOURNAL OF UROLOGY

Official Journal of the
British Association of Urological Surgeons



Volume 48 No 2

April 1976

E & S Livingstone

BRITISH JOURNAL OF UROLOGY

EDITOR
* W. KEITH YEATES

HON. TREASURER
* C. H. KINDER

ASSISTANT EDITORS
* G. D. CHISHOLM
* D. M. ESSENHIGH
* W. F. HENDRY
* W. SELBY TULLOCH

ASSISTANT EDITOR FOR AUSTRALASIA
G. F. MURNAGHAN

CONSULTING EDITORS
* DAVID BAND
* J. D. FERGUSSON

EDITORIAL COMMITTEE
Chairman D. INNES WILLIAMS*

G. H. BAINES, Birmingham
JOHN BALFOUR, Vancouver
D. R. BARNES, Cape Town
J. P. BLANDY, London
JEAN CHARBONNEAU, Montreal
C. A. C. CHARLTON, Bath
PHILIP CLARK, Leeds
B. N. COLABAWALLA, Bombay
M. H. DEVEREUX, Loughton, Essex
J. N. de KLERK, Cape Town
E. CHARLTON EDWARDS, Manchester
E. J. ENGLAND, Perth, W. Australia
H. FINE, Durban
ALBAN H. GEE, Sydney
N. O. K. GIBBON, Liverpool
JOHN GRIEVE, Dundee
A. R. HARRISON, London
D. K. KARANJAVALA, Bombay
J. A. KENNEDY, Belfast
W. K. KERR, Toronto
KENNETH J. MACKINNON, Montreal
J. W. F. MACKY, Auckland
JOHN P. MADDERN, Adelaide
J. P. MITCHELL, Bristol
*RICHARD A. MOGG, Cardiff
J. DERMOT O'FLYNN, Dublin
H. H. PEARSON, M.B.E., Canberra
J. S. PETERS, Melbourne
R. C. B. PUGH, London
P. J. M. RETIEF, Cape Town
CHARLES J. ROBSON, Toronto
L. STUART SCOTT, Glasgow
K. E. D. SHUTTLEWORTH, London
SARINDER MAN SINGH, Delhi
J. C. SMITH, Oxford
J. J. STEVENSON, London
J. H. STEYN, Aberdeen
W. BARR STIRLING, Glasgow
JOHN SWINNEY, M.C., Bunbury, W. Australia
G. C. TRESIDDER, London
P. J. P. VAN BLERK, Johannesburg
DAVID M. WALLACE, O.B.E., London
J. G. WATSON, Brisbane
R. H. WHITAKER, Cambridge
*J. L. WILLIAMS, Sheffield
J. F. R. WITHYCOMBE, Cambridge

* Members of Executive Committee

ST PETER'S MEDAL AWARDED TO

J. B. MACALPINE, 1949
R. OGIER WARD, 1951
TERENCE J. MILLIN, 1951
A. CLIFFORD MORSON, 1954
LESLIE N. PYRAH, 1959
CUTHBERT E. DUKES, 1960
DAVID BAND 1962
SIR ERIC RICHES, 1964

THE BRITISH ASSOCIATION OF UROLOGICAL SURGEONS

ARTHUR H. JACOBS, 1965
D. INNES WILLIAMS, 1967
H. HAMILTON STEWART, 1968
JOHN SWINNEY, 1969
SIR MICHAEL WOODRUFF, 1970
D. S. POOLE-WILSON, 1971
DAVID M. WALLACE, 1973
A. W. BADENOCH, 1974
HOWARD G. HANLEY, 1975

E. & S. Livingstone
Edinburgh and London
April 1976

Contents

UNIVERSITY
LIBRARY

ORIGINAL ARTICLES

93 **Diphosphonate Therapy in Nephrocalcinosis**
D. A. McCredie, H. R. Powell and E. Rotenberg

101 **The Surgical Management of Tuberculous Lower Ureteric Stricture**
P. J. O'Boyle, E. M. Galli and J. G. Gow

107 **Traumatic Avulsion of the Ureter with Obstruction, Pseudocyst Formation and Hypertension**
B. F. Ribeiro and J. K. M. Quartey

111 **Influence of Vesico-ureteral Reflux on the Response to Treatment of Urinary Tract Infections in Female Children**
William R. Fair and Duncan E. Govan

119 **Percutaneous Suprapubic Cystostomy after Spinal Cord Injury**
J. B. Cook and P. H. Smith

123 **Asymptomatic Phaeochromocytoma of the Bladder Co-existing with Carcinoma**
C. H. Leong, K. K. Wong and D. Saw

127 **Male Epispadias: Surgical Repairs of Urethropenile Deformity**
Emil A. Tanagho

135 **An Unusual Case of Right and Left Testicular Arteries Arching over the Left Renal Vein**
Hilel Nathan, Philip V. Tobias and Michael D. Wellsted

139 **A.I.D.—A Review of 200 Cases**
Robert Newill

SHORT CASE REPORTS

106 **A Complication of Nephrectomy by the Supracostal Approach**
Gordon Williams and J. E. Castro

118 **Bilateral Renal Carcinomas Treated Operatively**
Stefan Wesolowski

122 **Lymphocele following Renal Transplantation: an Unusual Cause of Urinary Retention**
Martin Schiff, Jr. and Robert A. Feldman

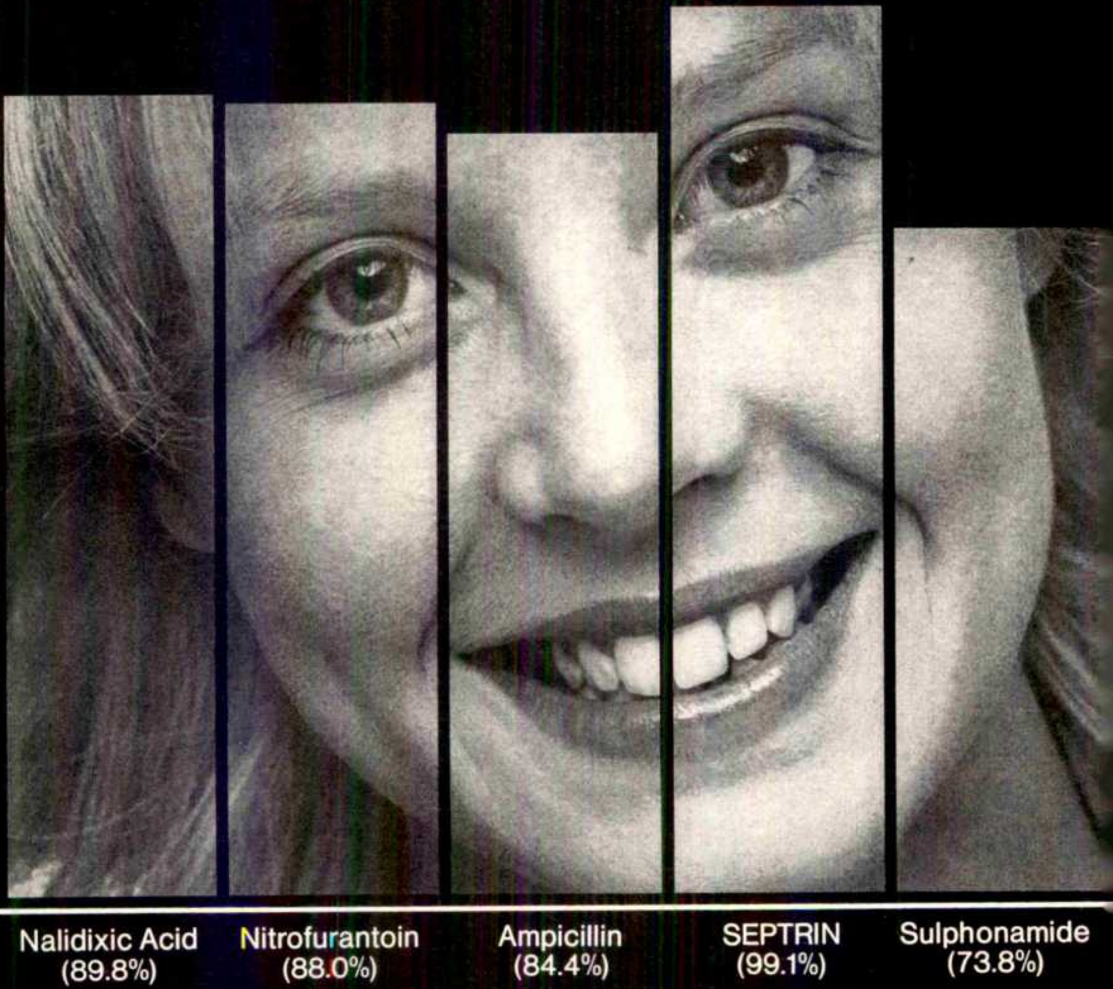
145 ABSTRACTS OF THE PROCEEDINGS OF THE UROLOGICAL SOCIETY OF AUSTRALASIA, 28TH ANNUAL GENERAL MEETING, SYDNEY, 1975

157 BOOK REVIEWS

158 BOOK RECEIVED and ANNOUNCEMENTS

ISSN 0007–1331

A 99.1% chance of success in U.T.I.



The chart above shows the percentage sensitivities of isolates from acute urinary infections against five commonly-used antibacterials. (From an *in-vitro* study involving 173 general practitioners). SEPTRIN was superior to all other oral antibacterials tested, with 99.1% of urinary pathogens sensitive

J int med Res (1974), **2**, 40

ome
ntains
rim and
thoxazole.
CRIBING
ON IS AVAILABLE
ST.
Medical Division
ome Foundation Ltd
ted, Herts

SEPTRIN first

TRADE MARK

in urinary tract infecti[illegible]n

Instructions to Authors

The *British Journal of Urology* welcomes original contributions on urological subjects from all parts of the world. The papers are accepted for consideration on the understanding that their contents have not been published in whole or in part elsewhere and that they are subject to editorial revision.

Any paper may be sent initially to a member of the Editorial Committee for comment and advice on its being suitable to be considered for publication.

A leaflet showing the criteria used in the assessment of papers submitted for consideration is available from the Editor on request.

Authors should supply their qualifications, main appointment, and the name and address of the hospital or the laboratory.

Please indicate name and address to which requests for reprints should be made.

Format and content of papers

The text of articles submitted for publication should be typewritten in double-spacing on paper sheet size 22 × 32 cm (A4). There should be a minimum margin of 3 cm all round. The pages should be numbered.

Reports on clinical or laboratory investigation should as far as possible be organised into the following main sections: (1) Introduction, (2) Objective(s), (3) Patients or Materials, (4) Procedures or Methods, (5) Findings or Results, (6) Discussion and (7) Conclusions with (8) a Summary at the end.

Nephrology. Papers on disorders of renal function of interest to the urological surgeon are welcome.

Ethics. When relevant, authors must include a statement on the ethical aspects of their research.

Reports of clinical cases should consist of the following sections: (1) Introduction, (2) Case Reports and (3) Comment with (4) a Summary at the end.

Reports on single cases. Papers reporting a single case are considered for publication as full papers only when the case has definite instructional value. The Introduction and Discussion should not be disproportionate to the case presentation. *An abbreviated version suitable for publication as a Short Case Report as an alternative must also be submitted.*

In all full papers the literature should be summarised as concisely as is consistent with establishing the necessary basis for new material. Discussions and Conclusions should be strictly limited to the results presented. Recapitulation from previous sections should be avoided whenever possible. Summaries should be composed of very brief statements about each of the main sections.

Headings. The relative importance of sub-headings should be clearly indicated.

Numbers. All numbers should be shown as figures rather than as words.

References. *The accuracy of references is the responsibility of the author.* Only papers closely related to the author's work should be referred to; exhaustive lists should be avoided. *References in the text* should be quoted by the author's name(s) and year of publication. Unless there are more than 3 authors, all the names should be stated at the first reference; if there are more than 3 authors only the first author plus *et al.* is used. In subsequent references to the same paper, *et al.* is used if there are more than 2 authors. *The list of references at the end of the paper* should be in alphabetical order. *References to journals* should include the name(s) and initials of the author(s), year, title of paper, name of journal in full, volume number and the numbers of the first and last pages, *References to books* should include the name and initials of the author, year, title of book, number of edition, city of publication, name of publishing house, and page number(s).

Illustrations. Photographs and radiographs should be submitted in the form of *matt* prints of a size no larger than 17·5 × 12·5 cm and no smaller than 9 × 6·5 cm. All figures should be sent unmounted. The number of the figure, the name of the author and the "top" of the illustration should be indicated lightly in pencil on the back. The magnification of micro-photographs should be stated. Graphs and diagrams should be drawn in Indian ink. *Lettering and figures must be indicated only on a transparent cover.* Legends to figures should be typewritten on a separate sheet of the manuscript. Tables, unless they are very small, should also be typewritten on separate sheets. The position of illustrations and tables should be indicated in the margin of the text.

There is no charge to contributors for the printing of black-and-white illustrations on papers accepted for publication. Illustrations in colour may be accepted at the discretion of the Editor provided he is of the opinion that these are necessary for the improvement of the article. The author may be required to pay for the extra cost involved by the reproduction in colour.

Reprints

25 offprints are supplied to the first named author only, free. Forms for ordering offprints will be sent with the proofs for correction; the order form should be returned with the corrected proofs within 7 days.

Continued on page v

Diet and renal stones. The inside story.

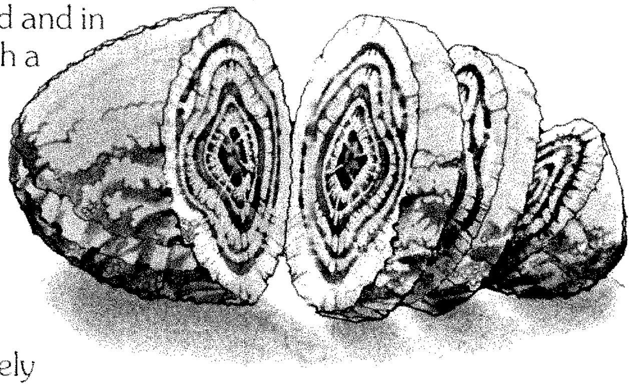
Traditionally, patients with idiopathic hypercalciuria have been treated with a low calcium diet.

Indeed, "A diet with a very low calcium content, less than 50 mg daily, should provide an effective method of controlling calciuria."[1]

However, "due to the presence of calcium in so many kinds of food and in drinking water, such a diet is hardly possible. It is not palatable and would lack many indispensable trace elements."[1]

Many foodstuffs contain a deceptively high level of calcium. A meal consisting of lamb stew can yield more calcium than the recommended allowance.[2]

This is why Whatman Sodium Cellulose Phosphate is being used increasingly as adjunctive treatment for idiopathic hypercalciuria. Whatman Sodium Cellulose Phosphate reduces calcium absorption and prevents renal stone formation.[3]



1. *Brit J Urol*, (1973), **45**, 136.
2. *Composition of Foods*, (1960), MRC Report 297, HMSO, London.
3. *American J Med*, (1971), **50**, 67.

Whatman®

Sodium Cellulose Phosphate

Fundamental treatment for idiopathic hypercalciuria.

Further information and data sheet on request from Whatman Biochemicals Limited,
Springfield Mill, Maidstone, Kent ME14 2LE. Telephone: Maidstone 673841. Telex: 96113.

® Registered trade mark of Whatman Limited

0651

Travelling Fellowship

The British Association of Urological Surgeons offers a Travelling Fellowship of £250 based on the best paper published in the *British Journal of Urology* in the preceding year including those papers presented at the British Association of Urological Surgeons Annual Meeting.

Candidates for the prize must be Fellows of one of the Royal Colleges of Surgeons in the British Isles, Canada, Australasia or South Africa who are in the course of urological training or who have obtained consultant posts within 10 years of the date of submission of the paper.

The Fellowship will be awarded for the best paper published in the Journal from the April issue of one year to the February issue of the following year.

Authors of papers with multiple authorship should indicate which one of their number should be awarded the Fellowship in the event of their contribution being selected.

Three assessors will be appointed by the Council to make recommendations on the award of the Fellowship. The Council reserves the right not to make an award in any one year.

The award will be announced at the June meeting of the Association.

Short Case Reports

Brief reports (preferably with 1 and not more than 2 illustrations) of unusual cases not published elsewhere may be submitted as summaries of not more than 200 words for consideration for publication as Short Case Reports. They should comprise (1) a Title, (2) Case description and (3) a brief Comment. The authors and references are each limited to 3. The titles of these reports will usually be recorded in Index Medicus and by MEDLARS.

Preliminary Communications

Preliminary communications of original work may be submitted as short papers. The communication should be divided into 4 sections: (1) Objectives, (2) Materials and Methods, (3) Preliminary results, (4) Interpretation or Significance of Results.

Discussion of Papers

Questions or criticisms concerning recently published paper may be sent to the Editor, who will refer them to the authors. The readers' comments and authors' replies may subsequently be published together.

There is no other correspondence section in the Journal.

Suggested Projects for Urological Research

Clinicians who have ideas for research projects, but have no opportunity for carrying them out, may submit them for publication in the above section. The communication should not be longer than 500 words. References will be limited to 6.

Abstracts from Current Urological Literature

Urologists who are willing to undertake abstracting of urological articles appearing in other journals should communicate with the Assistant Editor, Mr. W. Selby Tulloch, at the Department of Urology, Western General Hospital, Edinburgh, EH4 2XU.

Addresses

With the exceptions noted below, all editorial communications, including books for review, should be addressed to the Editor, Mr. W. Keith Yeates, at the Department of Urology, Newcastle General Hospital, Newcastle upon Tyne, NE4 6BE.

Preliminary Communications on Research Projects and *Suggested Projects for Urological Research* should be submitted to the Assistant Editor, Mr G. D. Chisholm, at The Urology Unit, Hammersmith Hospital, Royal Postgraduate Medical School, London, W12 0HS.

Short Case Reports (presented as described above) should be sent to the Assistant Editor, Mr W. F. Hendry, Institute of Urology, University of London, 172 Shaftesbury Avenue, London, WC2H 8JE.

Communications concerning the Abstract Section should be sent to the Assistant Editor, Mr W. Selby Tulloch, at the Department of Urology, Western General Hospital, Edinburgh, EH4 2XU.

Publishing, Advertisement and other enquiries: E. & S. Livingstone, Longman Group Ltd., Journals Division, Longman House, Burnt Mill, Harlow, Essex CM20 2JE.

Subscriptions

The Journal is published in February, April, June, August, October and December. Subscription £17·00 (U.S.A. $45.00) per annum, post free. Single copies £3·00 (U.S.A. $9.00) each. Previous volumes and parts of volumes (if available) may be obtained from the publishers, price £6.00 per volume or 75p for single parts.

Subscription enquiries: Messrs E. & S. Livingstone, Journals Division, 43/45 Annandale Street, Edinburgh, EH7 4AT.

Subscriptions for U.S.A. should be sent to The Williams and Wilkins Company, 428 East Preston Street, Baltimore, Maryland, U.S.A.

All rights reserved. No part of this publication may be reproduced, stored in a retrieval system, or transmitted in any form or by any means, electronic, mechanical, photo-copying, recording or otherwise, without the prior permission of the copyright owner.

Powerful output

Solid state generators in the DIADON 400 provide sufficient power for all types of surgery.
400 watts continuous cutting power, sufficient for even the most difficult underwater transurethral resection.
400 watt pulsed coagulation power (150 watt mean) sufficient to deal with all normal bleeding points encountered, even under water.
Individual output controls for cutting and coagulation allow smooth and accurate adjustment of output.

Pneumatic footswitch

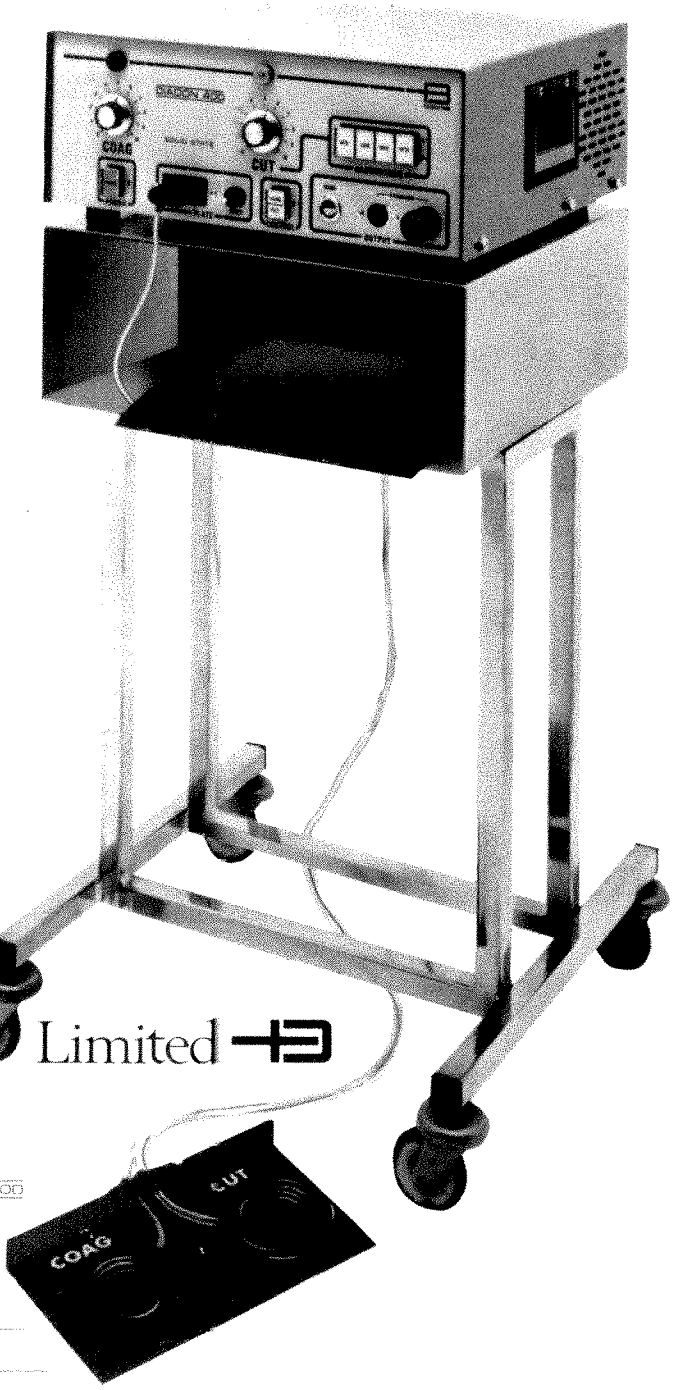
To completely eliminate all electric current from the floor the DIADON 400 is fitted with a pneumatic footswitch. This provides complete safety where water and flammable gases are present.
The footswitch gives separate control for both the cutting and coagulation functions.

Optional hand control

The DIADON 400 provides facilities to enable the use of the DIADON hand control which eliminates the footswitch and gives the surgeon complete control of the cutting and coagulation functions at his fingertips.
The DIADON hand control takes the normal range of electrode tips and may be autoclaved or immersed in fluid.

Made to HTM8

The DIADON 400 is constructed in accordance with the Department of Health and Social Security safety recommendations HTM8.



Downs Surgical Limited

Complete coupon for an illustrated leaflet on the DIADON 400 and post to Downs Surgical Limited, Mitcham, Surrey CR4 3UE.

Name ....

Address ....

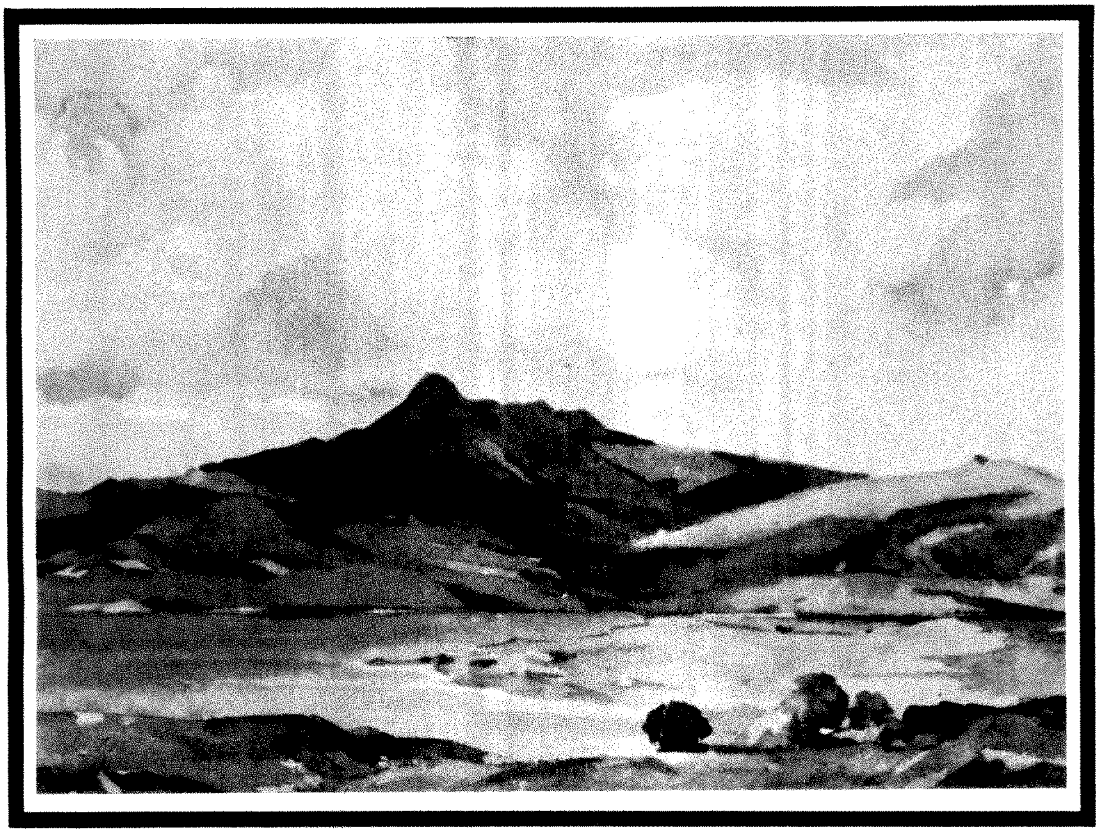
....

....

in radiography

conray contrast media

provide a distinctly better prospect all round



There is a wide range of 'Conray' formulations and almost certainly one to meet your special requirements however exacting they may be. 'Conray' provides wide margins of safety for the patient and superb visualization in a comprehensive range of radiographic procedures.

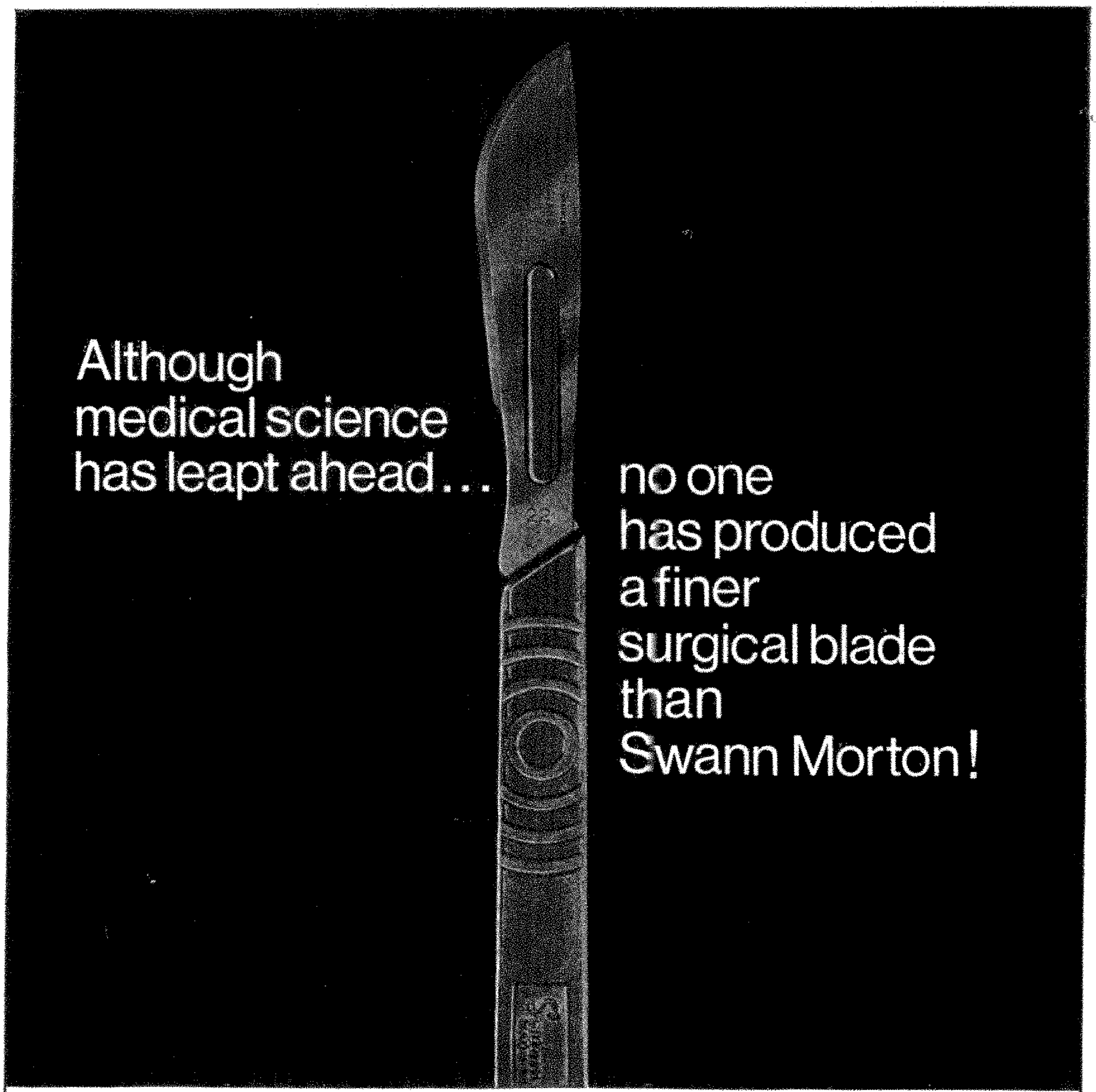
'Conray' Contrast media are preparations of meglumine iothalamate, sodium iothalamate or combinations of the two.

Further information on 'Conray' 280, 'Conray' 325, 'Conray' 420, Cardio-'Conray', Retro-'Conray' and Gastro-'Conray' supplied on request.
'Conray' is a trade mark of Mallinckrodt Inc.

May & Baker Ltd.
Dagenham, Essex RM10 7XS

M&B May&Baker
A member of the Rhône-Poulenc Group of Companies

MA 4334



Swann-Morton, the world's largest producers of surgical blades have kept abreast of the extremely high demands in surgical fields. Safe, stable and economical, their blades are sterilized by gamma radiation packed in quick peel foil envelopes and of a superb quality yet to be beaten.

STERILIZED
CARBON STEEL BLADES

STERILIZED
STAINLESS STEEL BLADES

STANDARD
CARBON STEEL BLADES

STERILE DISPOSABLE
STITCH CUTTERS

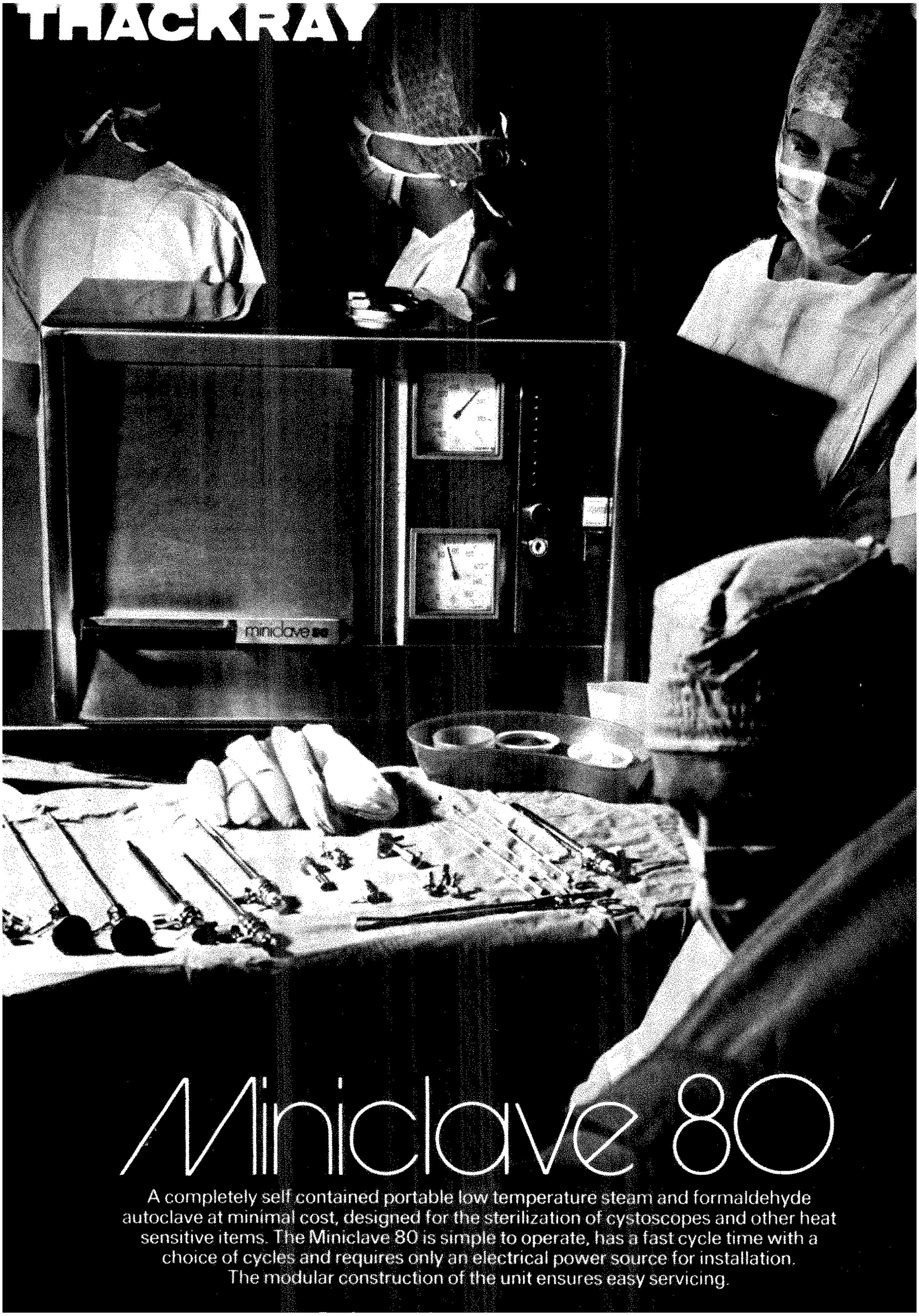
SURGICAL HANDLES

AUTOCLAVABLE PLASTIC
SURGICAL HANDLES

Swann-Morton

Surgical Blades

SWANN-MORTON LIMITED
PENN WORKS, OWLERTON GREEN,
SHEFFIELD S6 2BJ. ENGLAND



Miniclave 80

A completely self contained portable low temperature steam and formaldehyde autoclave at minimal cost, designed for the sterilization of cystoscopes and other heat sensitive items. The Miniclave 80 is simple to operate, has a fast cycle time with a choice of cycles and requires only an electrical power source for installation. The modular construction of the unit ensures easy servicing.

CHARLES C THOMAS • PUBLISHER

THE RENAL UPTAKE OF RADIOACTIVE MERCURY ($^{197}HgCl_2$): Method for Testing the Functional Value of Each Kidney, Technique–Results–and Clinical Application in Urology and Nephrology *edited by* **Claude Raynaud**, *Service Hospitalier Frederic Joliot, Orsay, France. Foreword by* **Pierre Royer.** *(41 Contributors)* Several techniques of uptake measurement are described along with simplified systems of external counting, scanners or gamma cameras. Normal values of Hg renal uptake as well as the results obtained in patients are outlined. The test described is easy to use, accurate and can be repeated with the same patient. Among topics discussed are corrections for organ depth and various types of instruments used. *'76, 248 pp., 110 il., 47 tables, $22.75*

CANCER EPIDEMIOLOGY AND PREVENTION: Current Concepts *edited by* **David Schottenfeld,** *Memorial Sloan-Kettering Cancer Center, New York. (23 Contributors)* An introductory section examines historical landmarks in cancer epidemiology, the magnitude of cancer, principles of the epidemiologic method, and cause. Subsequent sections cover etiologic agents, Burkitt's lymphoma, Hodgkin's disease, leukemia, cancers of specific tissues, screening and early detection, preventing disability, rehabilitation, colostomy, amputation, and neurologic disability. *'75, 592 pp. (6 3/4 x 9 3/4), 148 il., 86 tables, $45.50*

PURCHASING FOR THE HEALTH CARE FACILITY *by* **John H. Holmgren,** *St. Joseph Medical Center, Wichita, Kansas.* There is a need today for an understanding of health facility purchasing. This book was written to answer that need. It covers the major areas of purchasing from stores and inventory to negotiation and planning. Ways of reducing costs and purchasing are suggested and information is included on inventory, relations with vendors, negotiation, the departmental manual, traffic and transportation, health care purchasing as a profession, and future trends in health care material management. *'75, 288 pp., 18 il., 29 tables, $18.50*

CLINICAL USE OF DRUGS IN RENAL FAILURE *by* **Robert J. Anderson,** *Univ. of Colorado, Denver;* **John G. Gambertoglio,** *Univ. of California, San Francisco; and* **Robert W. Schrier,** *Univ. of Colorado, Denver.* With the advent of hemodialysis as a method of sustaining life there has been increased study of drugs used in the treatment of renal failure. This volume is a comprehensive drug reference source including in its discussion the pharmacology, adverse effects, dialysis properties and appropriate dosage modifications required for renal failure patients. *'76, 246 pp., 1 il., 18 tables, $19.50*

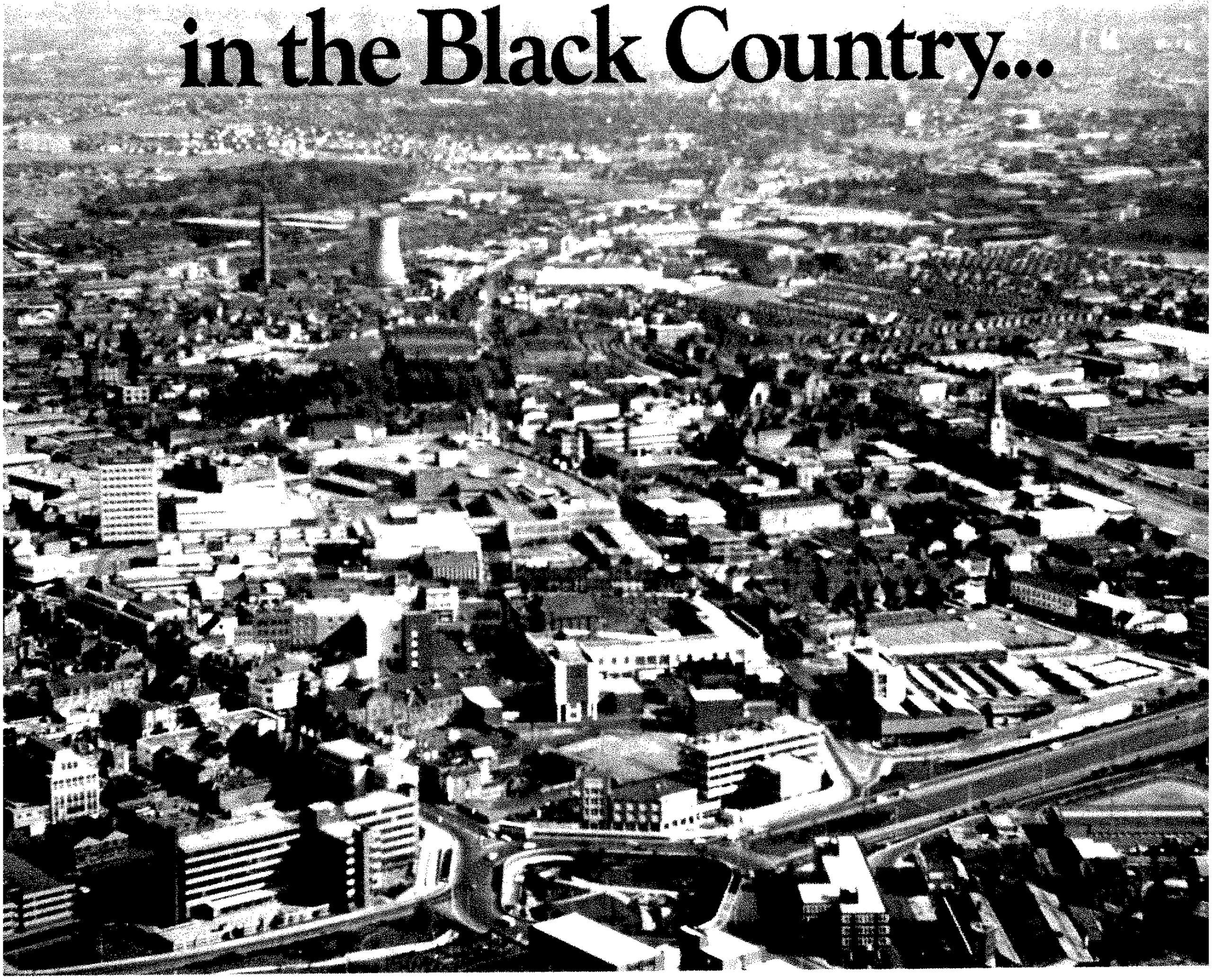
COMMON DUCT STONES *by* **Frank Glenn,** *Cornell Univ. Medical College, Ithaca, New York.* Specific consideration is given to when to anticipate common duct calculi, preoperative diagnosis of common duct calculi, diagnosis of common duct calculi at operation, and avoidance of retained calculi through use of the above three steps. Also discussed are what to do when postoperative T tube cholangiography suggests retained calculi and what to do when retained calculi are demonstrated. Successes and failures using solvents and instruments in removing retained calculi are reported. *'75, 148 pp., 22 il., 5 tables, $11.50*

UNDERSTANDING YOUR NEW LIFE WITH DIALYSIS: A Patient Guide for Physical and Psychological Adjustment to Maintenance Dialysis *by* **Edith T. Oberley** *and* **Terry D. Oberley,** *both of Univ. of Wisconsin, Madison. Forewords by* **Francesco del Greco** *and* **Eli A. Friedman.** This composite picture of vital technical, physical, psychological and philosophical material on understanding life with dialysis is written for patients, their families and professionals in the field. Chapters deal with physical and psychological preparation for dialysis, diet and medication, and many other topics. Photographs and stories of patients, technical photographs, and tables of important information such as food values give added impact. *'75, 160 pp., 26 il., 2 tables, cloth-$12.50, paper-$7.95*

Orders with remittance sent by air, postpaid

301-327 East Lawrence Avenue • Springfield • Illinois • 62717 • USA

Amoxil making all the difference in the Black Country...

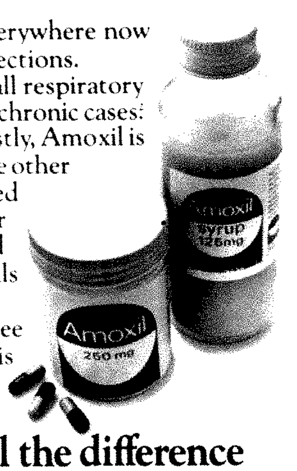


And throughout Britain. Because doctors everywhere now recognise the advantages of Amoxil in respiratory infections.

Amoxil ensures faster relief of symptoms[1] for all respiratory patients and longer periods free from infection for the chronic cases[2]

Three main factors are responsible for this. Firstly, Amoxil is more completely absorbed into serum[3] Secondly, unlike other antibiotics it penetrates equally well through inflamed and uninflamed bronchial membrane barriers[4] to clear even the most entrenched pockets of infection[5] And thirdly, extensive studies have shown that Amoxil kills bacteria more rapidly than other antibiotics[6,7]

These three factors, together with a trouble-free dosage, contribute to the Amoxil difference which is appreciated by doctors and patients everywhere.



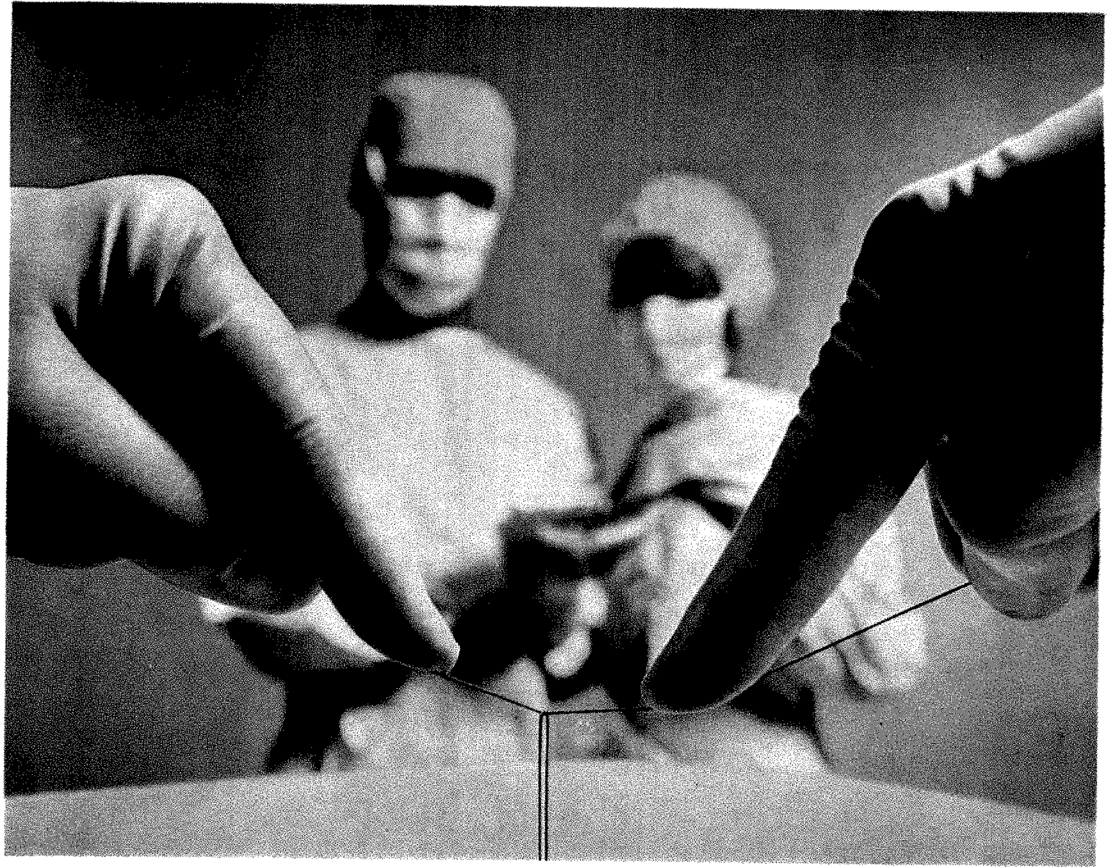
makes all the difference in respiratory infections everywhere.

1. Practitioner (1974), **212**, 123.
2. Chemotherapy (1973), **18**, (Suppl.) (19), 1
3. Br. Med. J., (1972), **3**, 11.
4. Excerpta Med. I.C.S. (1974) No. 326, 130.
5. S.A. Med. J., (1973), **47**, 719.
6. Antimicrob. Ag. Chem. (1975), **7**, (2), 179.
7. 'Antibiotics under the Microscope.' A film freely available to the medical profession.

Full prescribing information on Amoxil (regd.), amoxycillin, is available from Bencard, Great West Road, Brentford, Middlesex.

Bencard

Monofilament Smooth



Because of the even diameter of ETHICON* Surgical Gut along its entire length, the smooth monofilament surface finish makes passage through tissue easier and smoother and produces less trauma.

Catgut beds down smoothly and securely with even the first throw of the knot and holds securely and strongly with standard surgical knots.

But we're not stopping there. Through research and development we continually strive to offer you, the surgeon, the finest absorbable suture available—but that's only some of the reasons why ETHICON surgical gut is today's most widely used suture material.

Catgut places a world of experience at your fingertips.

ETHICON

When the difference is between being sure and being absolutely certain.

PLR 0508/5002

© ETHICON Ltd 1976 *Trademark

British Journal of Urology (1976), **48**, 93-100 ©

Diphosphonate Therapy in Nephrocalcinosis

D. A. MCCREDIE, H. R. POWELL and E. ROTENBERG
Department of Paediatrics, University of Melbourne and The Royal Children's Hospital, Melbourne, Australia

The inhibiting effect of diphosphonates on calcification in tissues has led to their successful use in conditions associated with abnormal calcification, such as myositis ossificans (Bassett *et al.*, 1969; Cram *et al.*, 1971; Weiss, Fisher and Phang, 1971; Russell *et al.*, 1972) and Paget's disease of bone (Smith, Russell and Bishop, 1971; Altman *et al.*, 1973; Russell *et al.*, 1974). *In vitro* experiments have shown that diphosphonates inhibit the crystallisation of calcium phosphate and calcium oxalate from solutions of these salts (Francis, 1969; Fraser *et al.*, 1972) and the disodium salt of ethane 1-hydroxy-1,1-diphosphonate (EHDP) inhibited the formation of calcium stones in rats with experimental nephrolithiasis (Fraser *et al.*, 1972). Few clinical studies have been reported on the use of diphosphonates in human stone-formers or patients with nephrocalcinosis, but it appears that inhibition of crystal growth may be obtained (Ohata and Pak, 1973; Baumann *et al.*, 1974; Robertson *et al.*, 1974). Whilst Uttley *et al.*, (1975) have recently reported the use of diphosphonates in 3 children with ectopic calcification in skin and subcutaneous tissues, their use in children with renal calcification has not been reported to our knowledge.

This paper presents results obtained with the use of EHDP in 4 children with nephrocalcinosis over a 13-month period. Preliminary results of these studies have been previously presented (McCredie, Powell and Rotenberg, 1974).

Methods of Study

3 children with Bartter's syndrome and hypercalciuria and 1 with hyperoxaluria were studied. Details of these patients are shown in Table I and a fuller account of the children with Bartter's syndrome has recently been published (McCredie, Williams and Rotenberg, 1974). 1 of the patients with Bartter's syndrome (Case 1) also had recurrent urinary infections and a small renal calculus. For several years prior to commencing EHDP 3 patients had been receiving oral magnesium supplements in an attempt to reduce the tendency to calcium oxalate precipitation (Dent and Stamp, 1970), whilst the child with oxalosis was also on supplemental sodium and potassium salts and frusemide, in an attempt to prevent calcium oxalate precipitation by maintaining an isotonic urine and medullary interstitium. These forms of treatment were continued unchanged during the trial of EHDP.

Table I

Details of Patients prior to Treatment with EHDP

Case	Age and sex		Height cm	Weight kg	Urine calcium mmol/d	Urine oxalate mmol/d
1	11 10/12	M	121·5	20·4	7·0	0·56
2	12	F	127	23·3	5·0	0·64
3	7 2/12	F	114	17·8	3·1	0·51
4	6½	M	110	22·7	1·5	2·39

Table II

Daily Protein and Mineral Intake of Patients

Case	Protein g	Calcium mmol	Phosphorus mmol	Magnesium mmol	Sodium mmol
1	35	10	21	18*	26
2	40	13	35	21*	15
3	65	18	39	13	30
4	36	12	25	24*	164†

* Including magnesium chloride supplementation.
† Including sodium chloride supplementation.

The children were admitted to a metabolic ward several days before commencing EHDP treatment and were kept on a diet of approximately constant composition which was as close as possible to their normal diet. Details are shown in Table II. Urine specimens were collected over two 24-hour periods, and calcium, magnesium, phosphate, creatinine and oxalate were measured. Serum levels of calcium, phosphorus, magnesium, creatinine and alkaline phosphatase were also measured. Radiography of left wrist and knee and radiotomography of the renal areas were performed. Care was taken, during tomography of the renal areas, to use the same machine and, as near as possible, the same factors for exposure and depth of tomography cut.

After the control studies EHDP treatment was begun. Approximately 10 mg per kg body weight was given as a single daily dose before breakfast. This amounted to one 200 mg tablet per day. In all patients 24-hourly urine collections were continued over the following 5 days, after which further serum estimations were made.

Studies were repeated at 1, 4, 7, 10, and 13 months. After 10 months EHDP dosage was increased to 400 mg/day in patients 1 and 4 and an additional study performed 1 month later. A right iliac crest trephine biopsy was performed in patients 1 and 4 after 11 months of treatment with EHDP, including 1 month on 20 mg/kg per day. The specimen obtained was embedded in Spurr's epoxy resin and sections of 3 μ thickness were examined by the

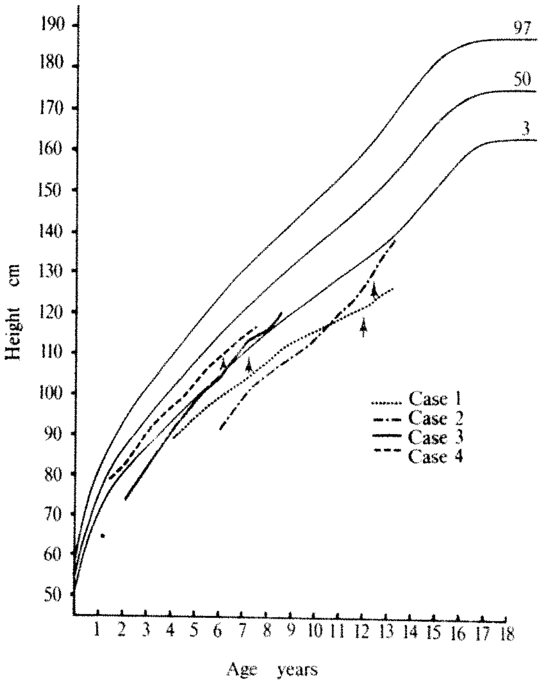


Fig. 1. Height graph of patients on EHDP. The arrows indicate time of onset of treatment. Curves of 3rd, 50th and 97th centiles for boys are shown for comparison.

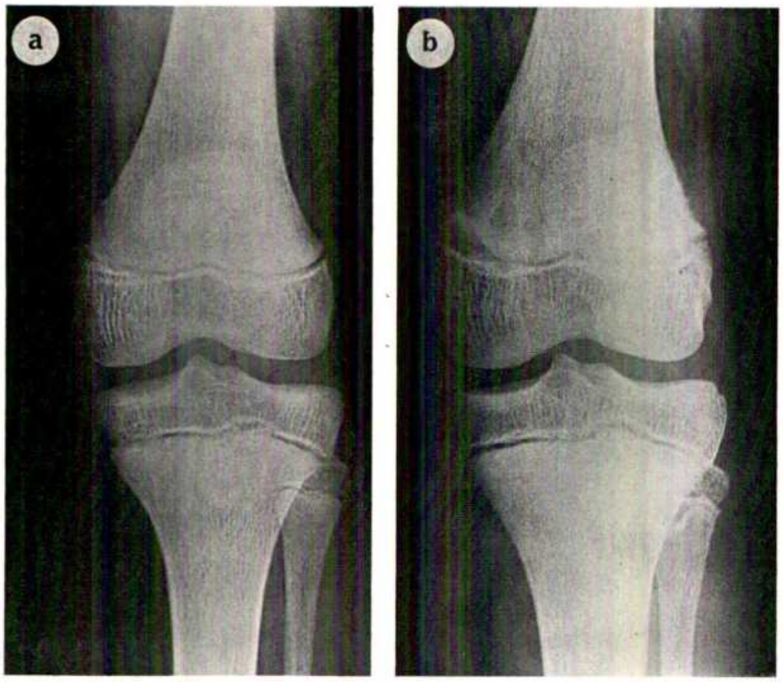


Fig. 2. X-rays of knees in Case 2. (a) Before treatment; (b) After 16 months EHDP, showing early changes of osteitis fibrosa cystica.

technique of Xipell, Makin and McKinnon (1974). Serum and urine calcium and magnesium were estimated by atomic absorption spectrophotometry, phosphorus by the method of Fiske and Subbarow (1925), urine creatinine by the Yaffe reaction and serum creatinine by the method of Edwards and Whyte (1958). Urinary oxalate was measured by a modification of the method of Zarembski and Hodgkinson (1965).

Crystallographic analysis of the calculus removed from Case 1 was performed using an X-ray diffraction technique (Lonsdale, Sutor and Wooley, 1968).

Results

All children remained clinically well with no new symptoms during the 13-month period of study.

Growth proceeded normally with height increasing at the same rate as before treatment, except in Case 2 where a pubertal growth spurt occurred (Fig. 1).

Skeletal age increased in proportion to chronological age in all children. Radiography of long bones showed no change in bony architecture during the 13 months of the study but with continuation of EHDP for a further 3 months in Case 2, some early changes of osteitis fibrosa cystica had appeared (Fig. 2). X-ray tomography of renal areas showed no clear change in calcification in Cases 2, 3 and 4 (Fig. 3). A considerable increase in size of the calculus occurred in Case 1 (Fig. 4) and a stone containing only magnesium ammonium phosphate was subsequently removed from the renal pelvis.

No significant change occurred in haemoglobin, or serum urea, creatinine, magnesium, glutamic-oxalacetic transaminase or protein levels at any time (Table III). There was a consistent small decrease in serum calcium levels within the first few days of treatment and this tended to persist throughout the ensuing 13 months. At the same time serum phosphorus rose and remained high, whilst alkaline phosphatase levels rose early and continued to rise. Table IV depicts changes in renal excretion. Urine volume and creatinine excretion showed no consistent change. Urine calcium excretion rose gradually to a mean level 30% higher than control during the study, while phosphate excretion tended to rise initially and then decreased to pre-treatment levels. The mean calcium : creatinine clearance ratio increased from 0·022 to 0·034 over the 13-month period, whilst the phosphorus : creatinine clearance ratio fell from 0·126 to 0·116. Urinary magnesium was unchanged initially but decreased during the second 6 months.

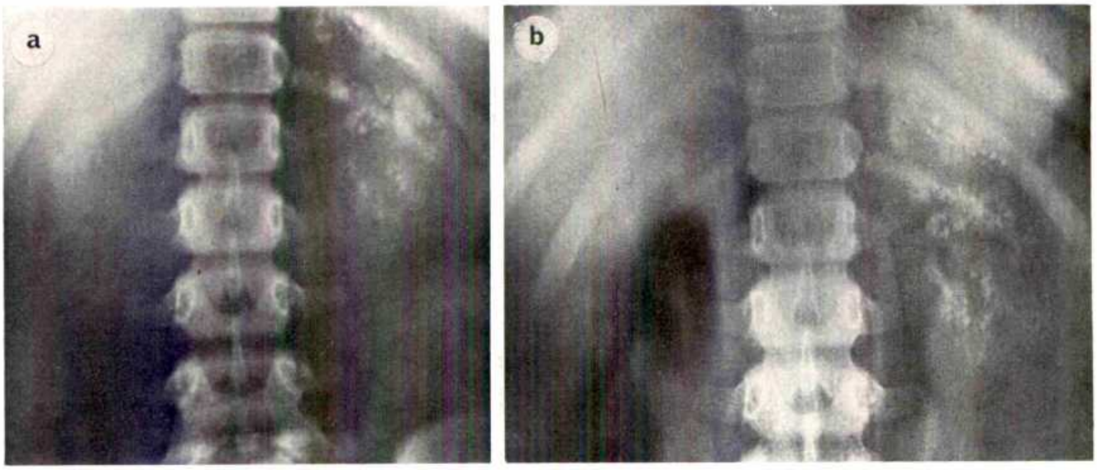


Fig. 3. Nephrotomography before (above) and after 13 months treatment in Case 3.

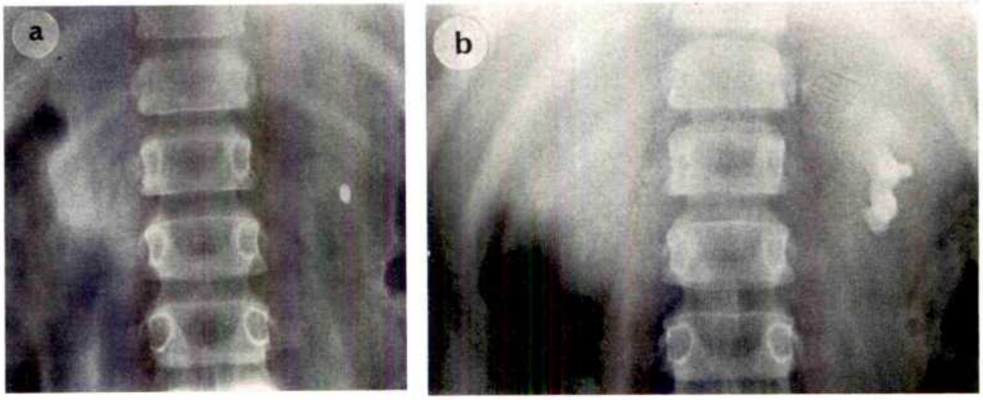


Fig. 4. Nephrotomography. (a) Before; (b) After treatment in Case 1. Note the considerable growth of calculus.

Oxalate excretion was not significantly affected. Creatinine clearance was normal in all children but fell from a mean value of 116 ml/min/1·73 m to 92 ml/min/1·73 m^2.

Intestinal absorption of a single dose of oral ^{47}Ca fell from an abnormally high level of 98% of the administered dose in patients 1 and 2 to 71% and 81% respectively after 8 and 10 months on EHDP despite comparable dietary calcium intakes.

Bone biopsy performed in Cases 1 and 4, after 1 month's treatment with the higher dose of EHDP, showed moderately thickened osteoid seams covering a greater proportion of the bony trabeculae, with some small areas of increased resorption in Case 1.

Discussion

EHDP in the dosage used in this study produced no clinical ill-effects and did not interfere with growth or skeletal maturation. However, some disturbance in bone metabolism was indicated by a consistent rise in serum alkaline phosphatase levels and by the presence of an excess of osteoid tissue coating bone trabeculae in 2 patients in whom bone biopsy was performed. Whilst this was not sufficient to produce clinical or radiological evidence of osteodystrophy in the first 12 months of treatment, radiographic signs had appeared in Case 2 after 16 months. Continued use for a more prolonged period might therefore be expected to produce more serious bony

Table III

Blood Chemistry of Patients on EHDP Treatment

Time after onset of treatment	Creatinine mmol/l	Calcium mmol/l	Phosphorus mmol/l	Magnesium mmol/l	Alkaline phosphatase K.A. units/100 ml
Control	0·06 (0·04-0·07)	2·58 (2·30-2·70)	1·6 (1·3-1·8)	0·92 (0·88-1·96)	19 (14-25)
4-5 days	–	2·48 (2·35-2·58)	1·8 (1·6-1·9)	0·88 (0·83-0·96)	23 (17-29)
1 month	0·06 (0·05-0·07)	2·48 (2·40-2·63)	1·8 (1·5-2·5)	0·92 (0·88-0·96)	24·5 (16-36)
4 months	0·06 (0·04-0·09)	2·50 (2·38-2·63)	1·8 (1·4-2·2)	0·96 (0·79-1·08)	24 (16-36)
7 months	0·04*	2·33 (1·95-2·60)	1·8 (1·5-2·4)	0·88*	27 (20-34)
10 months	0·06 (0·04-0·09)	2·43 (1·98-2·63)	1·7 (1·5-2·1)	0·88*	26 (15-35)
13 months	0·06 (0·035-0·07)	2·45 (2·35-2·55)	1·9 (1·6-2·1)	0·83 (0·75-0·88)	28 (17-36)

Figures represent mean serum values of all patients with range in brackets.
* 3 patients only.

changes. Fleisch and Bonjour (1973) have also observed radiological evidence of rickets in some children treated for myositis.

A rise in serum phosphorus in patients treated with diphosphonates has also been observed by others (Fleisch and Bonjour, 1973; Procter and Gamble Co., personal communication) who have found that in adults this is not associated with a change in serum calcium. The lowering of serum calcium in children, which we have observed, is in contra-distinction to the hypercalcaemia induced in rats given a higher dosage (Bonjour *et al.*, 1972; Krawitt *et al.*, 1974) where the effect is attributed to decreased bone accretion rate with a secondary fall in calcium absorption from the gut (Bonjour *et al.*, 1972). Calcium absorption in 2 of our patients showed a slight fall from pre-treatment values despite the absence of hyercalcaemia. More marked decreases in calcium absorption have been recently reported by Uttley *et al.* (1975).

The increased urinary calcium which we found presumably results from decreased calcium accretion by bone, as it occurred despite a decrease in intestinal absorption. As urinary calcium excretion was high initially in the patients with Bartter's syndrome a further increase must be viewed with some concern. However, further renal calcium deposition was not apparent in any of these children. The calculus in the renal pelvis in Case 1 enlarged during 16 months of EHDP treatment and was found to consist of pure magnesium ammonium phosphate (Struvite). The lack of effect of EHDP on the growth of such stones is well documented (Fraser *et al.*, 1972). Urinary infection was present in this case and *Proteus mirabilis* was grown from the calculus. Lowering of urine magnesium was a consistent finding and was noted also by Robertson *et al.* (1974). The cause of this is unclear.

The changes in blood and urine calcium and phosphorus are similar to those found in hypoparathyroidism. However, the increase in serum alkaline phosphatase and the pathological and radiographic (Case 2) evidence of increased areas of resorption suggest in fact that there is some degree of increased activity of the parathyroid gland. It is suggested that a direct renal effect of EHDP may result in decreased tubular reabsorption of calcium and increased reabsorption

Table IV

Urine Chemistry of Patients on EHDP Treatment

Time after onset of treatment	Volume ml	Creatinine mmol/d	Calcium mmol/d	Phosphorus mmol/d	Magnesium mmol/d	Oxalate mmol/d
*Bartter's syndrome**						
Control	2620 (1170-4000)	3·8 (3·3-4·6)	5·0 (2·8-8·2)	14·0 (11·9-16·5)	6·5 (4·2-10·8)	0·57 (0·48-0·74)
2nd and 3rd day	2860 (1530-4640)	3·9 (3·5-4·8)	5·1 (3·6-8·7)	15·7 (13·4-19·5)	6·3 (3·9-9·2)	0·69 (0·48-0·81)
1 month	2630 (1445-3220)	4·1 (3·3-4·6)	5·0 (2·4-6·8)	14·7 (11·9-18·9)	6·3 (3·4-9·4)	0·63 (0·48-0·84)
4 months	2900 (1520-4150)	4·3 (3·3-5·7)	5·5 (3·0-7·6)	15·3 (11·1-19·8)	6·0 (3·5-12·3)	0·58 (0·39-0·79)
7 months	3000 (1970-4150)	4·0 (3·7-4·7)	5·8 (3·9-8·6)	15·2 (11·1-19·5)	3·9 (2·5-5·0)	0·62 (0·34-0·81)
10 months	2970 (1675-4030)	4·0 (3·3-5·1)	5·6 (4·0-8·8)	13·2 (9·7-16·9)	4·8 (2·9-7·5)	–
13 months	2850 (1750-3750)	3·7 (3·0-4·6)	6·5 (4·4-8·9)	13·4 (12·1-15·0)	4·4 (2·6-7·5)	–
Hyperoxaluria†						
Control	3400	4·7	1·5	14·0	7·3	2·39
2nd and 3rd day	3400	4·2	1·6	14·5	6·5	2·56
4th and 5th day	3525	4·1	1·9	17·6	6·5	2·17
1 month	3310	4·8	2·5	17·3	6·7	2·22
4 months	2600	4·6	1·0	18·6	5·6	–
7 months	3440	4·0	2·5	15·0	5·8	–
10 months	3640	4·2	2·4	18·2	6·3	2·07
13 months	3530	4·7	3·0	15·5	5·6	–

* Figures represent mean excretion in all patients, 2 separate 24-hour collections being taken in each case. Range of values is shown in brackets.

† Figures represent mean of 2 24-hour urine collections.

of phosphorus. The gut absorption studies suggest that similar changes may occur in calcium and phosphorus transport across the intestinal wall. This would tend to produce hypocalcaemia and hyperphosphataemia with a secondary increase in parathyroid activity. Bone resorption would then predominate over bone accretion, which is reduced by diphosphonate (Cabanela and Jowsey, 1974) so that a combination of osteitis fibrosa cystica and osteomalacia may occur.

The absence of change in nephrocalcinosis and an actual increase in stone formation in 1 patient suggests a lack of benefit from EHDP therapy in nephrocalcinosis. As EHDP not only inhibits crystal growth but also acts as a crystal stabiliser one would not therefore expect a rapid decrease in areas of calcification and the principal value of diphosphonates may be in preventing further calcium crystal growth. The lack of progression of nephrocalcinosis then compares favourably with a definite increase observed in 2 children over the preceding 12 months. However, the rise in serum alkaline phosphatase and the histological and radiological evidence of a defect in osteoid mineralisation during diphosphonate therapy in this study, suggest that treatment for longer periods may not be tolerated without the development of significant bone disease.

Summary

4 patients with nephrocalcinosis were treated with disodium ethane 1-hydroxy-1,1-diphosphonate (EHDP) for a period of 13 months.

No clinical side-effects were observed and growth proceeded normally.

Radiographic changes of osteitis fibrosa cystica developed in 1 child and bone biopsy in 2 children showed defective osteoid mineralisation.

It is suggested that EHDP prevented further crystal deposition in 3 children but did not prevent non-calcium stone formation in the 4th child.

In view of this and the development of histological and radiographic evidence of osteomalacia and/or secondary hyperparathyroidism in these patients the value of EHDP remains dubious. On the other hand its use may be justified when rapidly increasing calcification is expected, as for example in hyperoxaluria.

We wish to acknowledge the assistance of Dr J. Xipell, Department of Pathology, Austin Hospital, Melbourne, for processing and interpretation of bone biopsy material, Mr J. Allpress, Department of Tribophysics, C.S.I.R.O., Melbourne, for crystallographic analysis of the calculus and Mr H. E. Davies, Department of Pathology, Royal Children's Hospital, Melbourne, for oxalate determinations. EHDP was supplied by Dr Blair Geho, Procter and Gamble Laboratories, Cincinnati, USA.

References

ALTMAN, R. D., JOHNSTON, C. C., KHAIRI, M. R. A., WELLMAN, H., SERAFINI, A. N. and SANKEY, R. R. (1973). Influence of disodium etidronate on clinical and laboratory manifestations of Paget's disease of bone. *New England Journal of Medicine*, **289**, 1379-1384.

BASSETT, C. A. L., DONATH, A., MACAGNO, F., PREISIG, R., FLEISCH, H. and FRANCIS, M.D. (1969). Diphosphonates in the treatment of myositis ossificans. *Lancet*, **2**, 845.

BAUMANN, J. M., GANZ, U., BISAZ, S., FLEISCH, H. and RUTISHAUSER (1974). Verabreichung eines Diphosphonats zur Steinprophylaxe. *Helvetica Chirurgica Acta*, **41**, 421-424.

BONJOUR, J. P., RUSSELL, R. G. G., MORGAN, D. B. and FLEISCH, H. A. (1972), Intestinal calcium absorption, Ca-binding protein and Ca-ATPase in diphosphonate treated rats. *American Journal of Physiology*, **224**, 1011-1017.

CABANELA, M. E. and JOWSEY, J. (1974). Effect of ethane 1-hydroxy-1,1-diphosphonate on bone turnover in adult dogs. *Clinical Orthopaedics*, **100**, 364-369.

CRAM, R. L., BARMADA, R., GEHO, W. B. and RAY, R. D. (1971). Diphosphonate treatment of calcinosis universalis, *New England Journal of Medicine*, **285**, 1012-1013.

DENT, C. E. and STAMP, T. C. B. (1970). Treatment of primary hyperoxaluria. *Archives of Disease in Childhood*, **45**, 735-745.

EDWARDS, K. D. G. and WHYTE, H. M. (1958). The measurement of creatinine in plasma and urine. *Australian Journal of Experimental Biology*, **36**, 383-394.

FISKE, C. H. and SUBBAROW, Y. (1925). The colorimetric determination of phosphorus. *Journal of Biological Chemistry*, **66**, 375-400.

FLEISCH, H. A. and BONJOUR, J. P. (1973). Diphosphonate treatment in bone disease. *New England Journal of Medicine*, **289**, 1419-1420.

FRANCIS, M. D. (1969). The inhibition of calcium hydroxyapatite crystal growth by polyphosphonates and polyphosphates. *Calcified Tissue Research*, **3**, 151-162.

FRASER, D., RUSSELL, R. G. G., POHLER, O., ROBERTSON, W. G. and FLEISCH H. (1972). The influence of disodium ethane 1-hydroxy-1,1-diphosphonate (EHDP) on the development of experimentally induced urinary stones in rats. *Clinical Science*, **42**, 197-207.

KRAWITT, E. L., SAMPSON, W. H., KUNIN, A. S. and MATTHEWS, J. L. (1974). Effect of ethane 1-hydroxy-1, 1-diphosphonate (EHDP) administration on duodenal calcium transport. *Calcified Tissue Research*, **15**, 21-29.

LONSDALE, K., SUTOR, D. J. and WOOLEY, S. E. (1968). Composition of urinary calculi by X-ray diffraction. Collected data from various localities. I. Norwich (England) and district, 1773-1961. *British Journal of Urology*, **40**, 33-36.

MCCREDIE, D. A., POWELL, H. R. and ROTENBERG, E. (1974), Diphosphonate therapy in nephrocalcinosis. *Australian and New Zealand Journal of Medicine*, **4**, 420.

MCCREDIE, D. A., ROTENBERG, E. and WILLIAMS, A. L. (1974). Hypercalciuria in potassium-losing nephropathy. *Australian Paediatric Journal*, **10**, 286-299.

OHATA, M. and PAK, C. Y. C. (1973). The effect of diphosphonate on calcium phosphate crystallization in urine *in vitro*. *Kidney International*, **4**, 401-406.

ROBERTSON, W. G., PEACOCK, M., MARSHALL, R. W. and KNOWLES, F. (1974). The effect of ethane 1-hydroxy-1, 1-diphosphonate (EHDP) on calcium oxalate crystalluria in recurrent renal stone-formers. *Clinical Science and Molecular Medicine*, **47**, 13-22.

RUSSELL, R. G. G., PRESTON, C., SMITH, R., WALTON, R. J. and WOODS, C. G. (1974). Diphosphonates in Paget's disease. *Lancet*, **1**, 894-898.

RUSSELL, R. G. G., SMITH, R., BISHOP, M. C., PRICE, D. A. and SQUIRE, C. M. (1972). Treatment of myositis ossificans progressiva with diphosphonate. *Lancet*, **1**, 10-11.

SMITH, R., RUSSELL, R. G. G. and BISHOP, M. (1971). Diphosphonates and Paget's disease of bone. *Lancet*, **1**, 945-947.

UTTLEY, W. S., BELTON, N. R., SYME, J., and SHEPPARD, H. (1975). Calcium balance in children treated with diphosphonates. *Archives of Disease in Childhood*, **50**, 187-190.

WEISS, I. W., FISHER, L. and PHANG, J. M. (1971). Diphosphonate therapy in a patient with myositis ossificans progressiva. *Annals of Internal Medicine*, **74**, 933-936.

XIPELL, J., MAKIN, H. and MCKINNON, P. (1974). A method for the preparation of undecalcified bone sections for light microscopy and microradiography. *Stain Technology*, **49**, 69-76.

ZAREMBSKI, P. M. and HODGKINSON, A. (1965). The fluorimetric determination of oxalic acid in blood and other biological materials. *Biochemical Journal*, **96**, 717-721.

The Authors

D. A. McCredie, MD, FRACP Nephrologist.
H. R. Powell, MRACP, Assistant Nephrologist.
E. Rotenberg, MBiolSc, Research Biochemist.

Correspondence to: Dr D. A. McCredie, Department of Paediatrics, Royal Children's Hospital, Melbourne 3052, Victoria, Australia.

British Journal of Urology (1976), **48**, 101-105 ©

The Surgical Management of Tuberculous Lower Ureteric Stricture

P. J. O'BOYLE, E. M. GALLI, and J. G. GOW
Liverpool Regional Urological Centre and Wrightington Hospital

At the present time genito-urinary tuberculosis is encountered infrequently in urological practice. 20 new cases of urinary tuberculosis were reported from the special unit at Wrightington Hospital in 1974, several of these being examples of advanced disease (O'Boyle and Gow, 1975).

The low ureteric stricture is a common problem in the management of this infection. The use of effective chemotherapy and improved radiology services have reduced the necessity for open surgical intervention, particularly in early cases. Consequently few urologists have the opportunity to evaluate the different surgical techniques of reimplantation of the ureter following excision of the tuberculous stricture.

The series reported here covers a 25-year period in the evolution of the operative treatment of lower ureteric stricture.

Clinical Material

During the period 1950-74 just over 1000 cases of genito-urinary tuberculosis were treated at Wrightington Hospital. 48 patients (5%) required surgical intervention due to stricture formation at the lower ureter. Table I shows details of clinical data. These were divided into 4 groups on the basis of surgical treatment which generally corresponded to the time intervals as noted.

1. 1950-56 Uretero-colic diversion—16 cases.
2. 1956-62 Direct ureteric reimplantation—12 cases.
3. 1962-70 Boari procedures—13 cases.
4. 1970-74 Reflux preventing reimplantation—7 cases.

With the exception of the first group, where the usual indication was a contracted bladder with or without active tuberculous cystitis the indications for surgical intervention were obstruction of the lower ureter by tuberculous stricture with progressive upper tract dilatation and impaired renal function. The diagnosis was confirmed in every case by serial pyelography and where possible by retrograde examination with delineation of the stricture. All had received a course of chemotherapy considered adequate at the time and several had had in addition a short course of steroids.

Ureterocolic Diversion 1950-56

16 patients were treated by this method. The ureters were reimplanted by the standard Leadbetter technique. The mean age at operation was 36 years (22-54). The majority had long standing extensive tuberculosis with a remarkable average duration prior to surgery of 10 years. The extensive pathology in these patients is underlined by the incidence of associated surgical procedures. In particular nephrectomy was required in 11 cases.

The results of treatment were correspondingly disappointing by modern standards. 14 patients died due to progressive renal failure in association with infection and metabolic imbalance. The mean survival time was 3 years, 10 months.

Table I

Details of Clinical Data

	Ureterocolic diversion	Direct reimplant	Boari procedure	Reflux preventing
No. of patients	16	12	13	7
Age of operation	36 yr (22-54)	35 yr (17-49)	38 yr (10-49)	38 yr (30-47)
Average duration of G.U.T.B. prior to operation	10 yr	1·75 yr	9 months	6 months
Associated surgical procedures:				
Nephrectomy	11	3	1	1
Epididymectomy	4	2	–	1
Capsulectomy	1	–	–	–
Partial nephrectomy	–	–	1	–

1 of the 2 remaining survivors died 11 years after surgery as a result of cerebral vascular disease. At that time his renal function was satisfactory and there was no evidence of residual tuberculosis. The other survivor is of particular interest and was the last patient treated by this method in the series. She was then aged 22 and had had symptomatic tuberculosis for only 1 year. 6 years later colocystoplasty was undertaken for severe recurrent urinary infection. Subsequently her renal function, though impaired, was controlled by dietary measures and ultimately dialysis. She finally received a successful renal transplant in 1973, 17 years after diversion, and remains well.

Direct Ureteric Reimplantation 1956-62

12 patients were treated by an oblique mucosa-to-mucosa direct anastomosis of the ureter to the fundus of the bladder. The mean age at operation was 35 years (17-49). There was a striking difference in duration of symptoms prior to surgery with a mean value of 1·75 years. This is reflected in the survival figure of 75%, 3 patients dying of chronic renal failure. These were the last deaths recorded in the series and each was associated with a non-functioning contralateral kidney.

1 of these developed gross vesico-ureteric reflux with intractable pyelonephritis in the remaining kidney. The remaining 2 patients developed stenosis at the site of the reimplantation with rapid deterioration of renal function. The 9 survivors had a significant complication rate. A third patient with re-stenosis was converted to a Boari procedure with an excellent result. 5 patients developed vesico-ureteric reflux and in 1 of these who had gross reflux a Boari procedure failed to preserve the kidney.

Significant postoperative urinary infection was noted in 4 patients, on 2 occasions associated with reflux. In the other 2 a persistent Proteus infection ultimately led to calculus formation.

Boari Procedures 1962-1970

13 patients were treated by procedures incorporating a Boari bladder flap. In 9 cases an oblique end-to-end vesico-ureteric anastomosis was performed and in 4 an antireflux submucous tunnel was used. This has been described in detail elsewhere (Gow, 1968).

The mean age at operation was 38 years (10-49). The mean duration of disease prior to surgery was 9 months and a corresponding decrease in associated surgery was noticed, only 1 patient requiring nephrectomy.

2 patients had previously had a direct reimplantation as noted above. The mortality of the procedure was nil. Significant postoperative complications were stenosis in 1 case with resultant

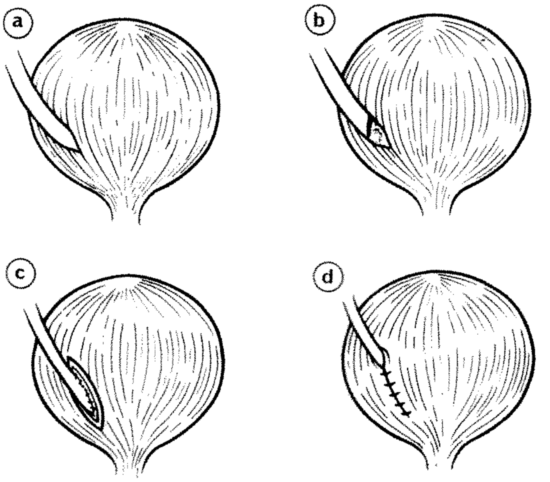


Fig. Diagrams of anti-reflux reimplantation technique: (a) Ureter positioning at any convenient site; (b) Ureter divided obliquely and myotomy performed; (c) Mucosa-to-mucosa anastomosis; (d) Reconstitution of bladder muscle to procure anti-reflux submucous tunnel.

loss of that kidney and urinary fistula formation on 3 occasions with the loss of 1 further kidney. It seems likely that fistula formation was due to a technical error in reconstituting the bladder and could have been avoided (Gow, 1968). Vesico-ureteric reflux was found invariably following direct end-to-end anastomosis. This was associated with urinary tract infection in 3 cases (30%) and in 3 cases with failure of upper tract dilatation to improve, though this had no demonstrable effect on renal function.

Reflux following the Boari procedure can be prevented when the condition of the ureter permits by a tailoring procedure with reimplantation via a submucous tunnel as described by Gow (1968). This was adopted in 4 of our cases, none of whom subsequently refluxed though 1 continued to have a persistent urinary infection.

Reflux Preventing Reimplantation

Since 1970 a simple and effective method of anti-reflux reimplantation of the ureter has been used whenever possible. Details are shown in the accompanying diagram. The ureter is positioned, trimmed obliquely and the bladder muscle fibres divided to expose the mucosa. This is incised and a mucosa-to-mucosa anastomosis achieved using 3/0 chromic catgut. The bladder muscle is finally reconstituted over the ureter with a continuous suture thus creating a submucous tunnel of approximately 5 cm in length depending on the size of the ureter. This technique is similar to the extravesical procedure described by Lich, Howerton and Davis (1961) who maintained the original ureterovesical junction.

This procedure has now been used in 7 cases with 1 failure due to stenosis. The average age at operation was 35 years with a mean duration of symptoms of 6 months. One exception described below has been excluded but otherwise associated surgery was minimal. There have been no postoperative complications and the results in terms of improvement in upper tract dilatation and absence of reflux seem very acceptable.

The 1 failure in this group represents an unusual situation. A nephro-ureterectomy had been performed in 1963 for tuberculosis and at that time he was noted to have a stricture of the lower ureter on the opposite side. Subsequently he had removed from the area and was referred to this hospital 10 years later with urinary symptoms referable to hydronephrosis. He had a particularly long stricture and might have been better managed in the first instance by a Boari procedure although any procedure was unlikely to be successful as pelvi-calyceal systems which have been dilated for such a period of time rarely return to normal.

Table II

Results of Treatment

	Reflux	Infection	Reduction of hydronephrosis
Direct reimplant (12 patients)	5	7	9
Boari procedure (13 patients)	9	4	10
Anti-reflux procedure (7 patients)	1	1	6

Results

These are summarised in Table II.

Discussion

It is not our intention to discuss the various manoeuvres which may avoid the necessity for open surgery. These have been fully described elsewhere and were the subject of extensive discussion at the Glasgow Symposium of the British Urological Association on Tuberculosis in 1969 reported subsequently in this journal. This series is concerned with the open surgical management of those ureteric strictures which had failed to respond to more conservative measures, including steroid therapy and ureteric dilatation, and in no way infers that the approach to tuberculous ureteric stricture should be exclusively surgical.

The uretero-colic diversion group is now mainly of historical interest and represents the results of treatment when anti-tuberculous chemotherapy was still at a relatively tentative stage. It has rarely any place in the modern management of genito-urinary tuberculosis. The results of treatment in this group indicate that diversion must be regarded as a palliative procedure rather than an attempt to restore renal function. These results were not surprising in view of the extensive pathology involved which might now be regarded as contra-indications to uretero-colic diversion.

The striking feature of the current ureteric reimplant era was the difference in the duration of symptoms of genito-urinary tuberculosis prior to surgery. This may be explained on the basis of effective chemotherapy and consequently an aggressive surgical policy. These cases largely eliminated the development of severe bladder dysfunction with the attendant necessity for diversion. The mortality in this group is attributed to the preoperative condition of these patients, all of whom had extensive disease with marginal reserve renal function. Nevertheless, the high morbidity associated with stenosis, infection and reflux must be regarded as unsatisfactory.

The Boari procedure is well established and safe with a minimal complication rate. Only 1 instance of re-stenosis was found in this group of 13 patients. The development of urinary fistula should not occur and it was significant that in the 3 cases encountered in this series the fistula was from the bladder which had been reconstituted with plain catgut, not from the anastomotic site. Since chromic catgut or PGA suture material have been used no further trouble has been encountered. The technique of direct end-to-end vesico-ureteric anastomosis must inevitably result in reflux and this has been our experience. It has been claimed that vesico-ureteric reflux is of little consequence in the adult kidney (Kerr *et al.*, 1970; Claridge, 1970). In this series, however, no less than one-third of cases showed significant recurrent urinary infection. Furthermore, the failure of radiological improvement in a further third of our cases suggests, that while no significant impairment of renal function has been detected in the presence of a good contralateral kidney, reflux should be avoided if possible. At that time the facility of isotope renography was not available but we feel that serial investigation would be useful in this situation.

In 4 cases which we have treated by tailoring of the ureter and submucous tunnelling there has been no reflux though 1 patient continues to have urinary infection.

The present technique of extravesical anti-reflux reimplantation has proved simple and effective. There has been only one failure in 7 patients treated this way and he represents a problem in that he had a rather long stricture and would have been better treated by the Boari method. A psoas hitch is invariably used at the site of entry of the ureter and it has not been our experience that kinking of the ureter during bladder filling presents a problem.

Summary

25 years' experience of the open surgical management of the lower ureteric stricture is reviewed.

An extravesical anti-reflux tunnel procedure has been found to be simple and effective.

There is still a place for the Boari procedure or psoas hitch, particularly in the management of a long stricture or when gross thickening of the ureter makes the formation of a tunnel of effective length impracticable.

References

Claridge, M. (1970). Ureteric obstruction in tuberculosis. *British Journal of Urology*, **42**, 688-692.

Gow, J. G. (1968). The results of the reimplantation of the ureter by the Boari technique. *Proceedings of the Royal Society of Medicine*, **61**, 128-130.

Kerr, W. K., Gale, G. L., Struthers, N. W., Peterson, K. S. S., Coulthard. H. S., Greatex, G. E., Cross, J., Wigle, W. D. and Ashley, M. D. (1970). Prognosis in reconstructive surgery for urinary tuberculosis. *British Journal of Urology*, **42**, 672-678.

Lich, R., Howerton, L. W. and Davis L. A. (1961). Recurrent urosepsis in children. *Journal of Urology*, **86**, 554-558.

O'Boyle, P. and Gow, J. G. (1975). Genitourinary tuberculosis: a study of 20 patients. *British Medical Journal*, **1**, 141-143.

The Authors

P. J. O'Boyle, MD, ChB, FRCS, Senior Surgical Registrar.
E. M. Galli, FFARCS, General Practitioner.
J. G. Gow, MD, ChM, FRCS, Consultant Urologist.

British Journal of Urology (1976), **48**, 106 ©

Short Case Report

A Complication of Nephrectomy by the Supracostal Approach

Turner-Warwick (1965) described many advantages of the supracostal approach to the kidney with rib preservation. Because of these advantages this incision has been used by one of the authors, without complication, for 5 years. We now report an unusual complication of the incision which resulted from incomplete mobilisation of the supports of the 12th rib.

Case Report

A 55-year-old male underwent left nephrectomy using a supra 12 incision. Recovery was complicated by a wound infection due to *Staph. aureus*. Despite appropriate antibiotics this developed into a sinus which was surgically explored 4 months later. A sequestrum of the tip of the 12th rib was removed, together with the remainder of the bone (Fig.). The patient made an uneventful recovery and the wound healed completely.

Pathological examination of the specimen showed active osteomyelitis, a sequestrum and cloaca.

Comment

The usual cause of persistent wound sinus after nephrectomy is infection associated with non-absorbable ligatures. Osteomyelitis of the rib has not been reported. In this case fracture of the rib followed incomplete division of the supracostal supports. If this is recognised during operation we would recommend excision of the rib fragment.

GORDON WILLIAMS and J. E. CASTRO

Urological and Transplantation Unit, Royal Postgraduate Medical School, Hammersmith Hospital, Du Cane Road, London W12 0HS

Reference

TURNER-WARWICK, R. T. (1965). The supracostal approach to the renal area. *British Journal of Urology*, **37**, 671-672.

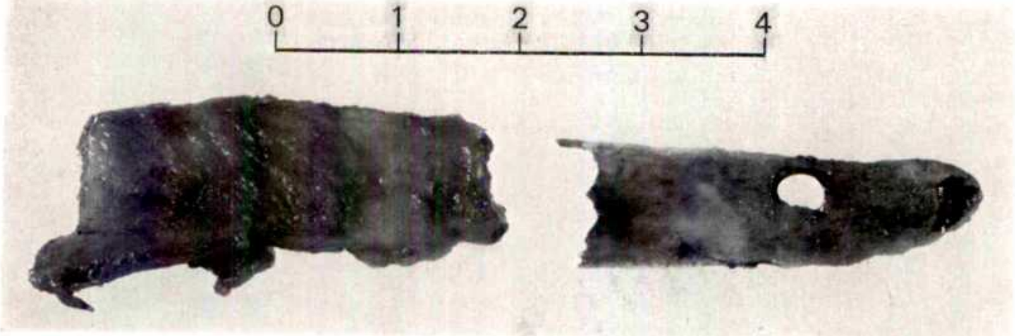


Fig. Excised 12th rib showing sequestrum with cloaca of the tip (R.H.S.).

British Journal of Urology (1976), **48**, 107-110 ©

Traumatic Avulsion of the Ureter with Obstruction, Pseudocyst Formation and Hypertension

B. F. RIBEIRO and J. K. M. QUARTEY
University of Ghana Medical School, Accra

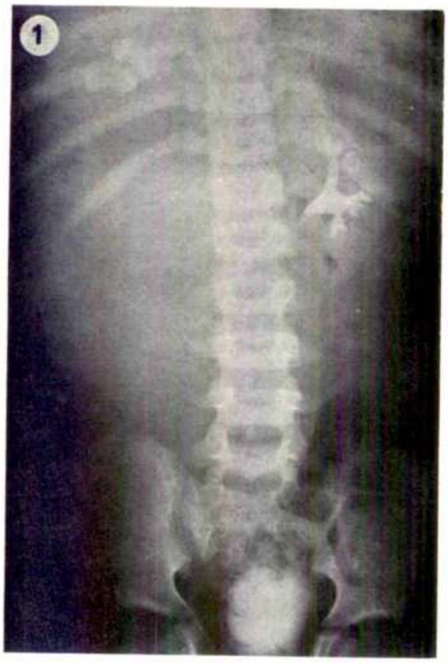
Traumatic avulsion of the upper ureter produced by blunt injury is not an excessively rare occurrence although a review of the literature reveals only 24 instances where the diagnosis has been substantiated at operation. We report a patient who developed renal outflow obstruction with pararenal pseudocyst formation following traumatic avulsion of the ureter at the pelvi-ureteric junction and was subsequently complicated by hypertension.

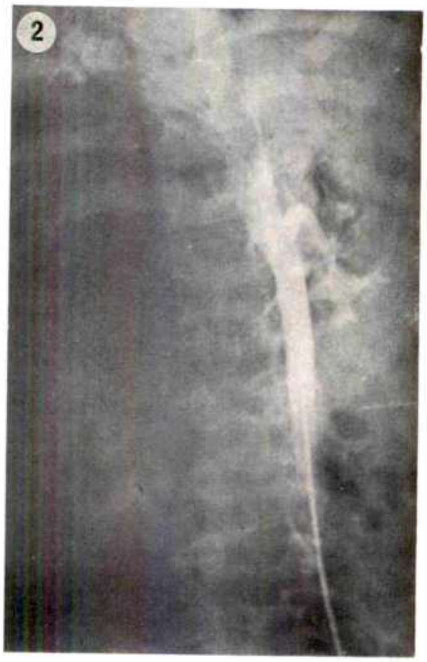
Case Report

A 12-year-old boy was admitted to Tamale Regional Hospital on 12 February 1974, following a fall from a tractor. He complained of pain in the abdomen and right hip and difficulty in passing urine. On examination there was an extensive graze over the left side of the abdomen with epigastric fullness and a distended bladder. His blood pressure was 90/60 mm Hg. A peritoneal tap was negative for blood or fluid. Chest X-ray was normal, X-rays of the pelvis showed a fracture of the superior and inferior pubic rami. A catheter was passed without difficulty; urinalysis revealed a few red blood cells and white cells. Following resuscitation and 24 hours of catheter drainage he passed urine spontaneously and without difficulty and his blood pressure returned to normal limits.

During the next 6 weeks he developed a swelling in the right hypochondrium. Initially tender, this became progressively larger and extended into the right iliac fossa. On intravenous pyelography (IVP) the right kidney was displaced upwards by the mass and hydronephrosis was apparent on the 20-min film (Fig. 1); the left kidney was normal. On 31 March he developed fits and vomiting and became semi-conscious. His blood pressure fluctuated between 150/130 and 190/140 and was treated with intravenous aldomet. 1 litre of serosanguinous fluid was aspirated from the mass with a marked reduction in size and a fall in his blood pressure to 140/100. 3 days later his blood pressure rose to 160/110 and he developed a right hemiparesis; further treatment with aldomet and epanutin reduced his blood pressure to 120/100. He was transferred to Korle Bu Teaching Hospital on April 16th; when seen, the vomiting had stopped and he had no urinary or bowel symptoms. On examination there was no evidence of a hemiparesis, the blood pressure was 135/90 and the apex beat was shifted to the left and thrusting in character. A large painless cystic mass occupied the whole of the right side of the abdomen. Blood urea was 26 mg % and haemoglobin 12·7 mg %. There were no red cells in the urine. 2 days after admission the patient became dyspnoeic and hypertensive and complained of headaches. Right retrograde pyelogram demonstrated a complete obstruction at the upper end of the ureter, which was displaced to the left of the midline. Again following aspiration of 1 litre of fluid from the cyst the blood pressure fell to 150/100 with some improvement in his dyspnoea and headaches. Analysis of the fluid confirmed it was sterile urine with a urea concentration of 78 mg % (blood urea 26 mg %). Chest X-ray showed enlargement of the heart with elevation of the diaphragm. A renal arteriogram showed the right kidney displaced upwards by the retroperitoneal mass and the renal artery stretched and thinned out over it (Fig. 2). A diagnosis of traumatic rupture with pseudocyst formation was made. A further hypertensive crisis occurred on 27 April with febrile convulsions and left-sided fits. This was treated with paraldehyde and digoxin.

On 7 May, at laparotomy, there was a right-sided retroperitoneal cyst displacing the right kidney high up under the liver and the intestines to the left, the kidney being rotated into a horizontal position. The ascending colon was stretched over the cyst and was dissected off it. The cyst was aspirated and dissected off the posterior abdominal wall. When the cyst was opened during dissection there was a small hole in its upper part through which urine was seen to be pouring. After excision of the cyst the hole was seen to be at the lower end of the pelvis from which the ureter had been completely avulsed. The upper end of the right ureter was freed from its adhesions on the posterior wall, mobilised and the stenosed end excised. The ureter was then spatulated and anastomosed to the pelvis with 0000 chromic catgut sutures. A nephrostomy tube was inserted and the wound closed in layers without drainage.





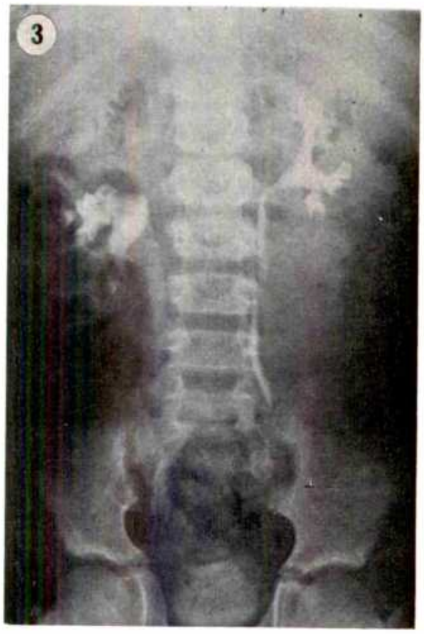


Fig. 1. Intravenous pyelogram about 1 month after injury. Displacement of the right kidney with hydronephrosis. Normal left kidney.

Fig. 2. Renal arteriogram, 9 weeks after injury showing stretching of the renal vessels by the pseudocyst.

Fig. 3. Intravenous pyelogram 6 months postoperatively showing good function of the right kidney which is slightly hydronephrotic.

The blood pressure fell to 120/80 on the 1st postoperative day and remained at this level until the patient was discharged from hospital. Pyelo-ureterogram through the nephrostomy tube on 16 May demonstrated adequate patency of the anastomosis, and the nephrostomy tube was removed. Recovery was uneventful. Renal arteriogram on 17 July showed the right renal artery in its normal position and of normal calibre. The patient was discharged on 27 July.

IVP 6 months postoperatively showed good function of the right kidney which was slightly hydronephrotic but draining well and with the right ureter well outlined (Fig. 3). The patient was well and normotensive.

Table

Ureteral Avulsion in 23 Patients

Age (range 2-74 years)	
Under 16 years	17
Over 16 years	5
Ureteral injury	
Right	12
Left	8
Bilateral	3
Diagnosis	
Early (within 24 hours)	11
Delayed	12*
Treatment (in 25 patients)	
Nephrectomy	4
Reanastomosis	21

* Range 3 days-10 weeks.

Discussion

A high degree of suspicion is necessary for a diagnosis of traumatic avulsion of the ureter, as initially there may be no physical signs suggesting trauma to the urinary tract. The presence of gross haematuria is exceptional although in most cases there has been some microscopic haematuria. This emphasises the need for an immediate IVP in such cases. A mass in the flank appears from a few days to many weeks after trauma, usually following earlier discomfort or pain in the flank. It may be tender at first but is usually non-tender when the patient is seen.

A "pseudocyst" or "urinoma" results from extravasation of urine from a partial or complete rupture of the ureter. An intravenous or retrograde pyelogram with aspiration and analysis of the fluid is diagnostic. Complete avulsion has been substantiated at operation in only 25 patients (including our 1 patient) (Bartley, Ekdahl and Wahlquist, 1966; Roe, 1969; Khonsari, Morehouse and MacKinnon, 1971; Del Villar, Ireland and Cass, 1972; Johnson *et al.*, 1972; Rao, 1973; Reznicheck, Brosman and Rhodes, 1973; Diokono, 1974; Boston and Smyth, 1975), details available on 23 patients are outlined in the Table. Reconstructive surgery is the treatment of choice when an early diagnosis is made. In 8 the diagnosis was delayed for more than 1 week, yet only 4 required nephrectomy.

In all reported cases avulsion from blunt injury occurs at or just below the pelvi-ureteric junction. In 12 patients (8 under 16 years old) it occurred flush with the pelvi-ureteric junction. The mechanism of injury is unclear, but extreme hyperextension and lateral flexion of the dorsal spine at impact may be responsible (Wilenius, 1950; Reznicheck *et al.*, 1973). The fact that the hydronephrotic pelvicalyceal system was so clearly seen on the 20-min IVP 1 month after injury is interesting for at such a stage of complete obstruction it would usually be indicated only by a nephrographic concentration; the continuation of urine excretion in this case is presumably the result of continuous reabsorption of urine from the wall of the pseudocyst.

Hypertension following parenchymal damage, lesions of the renal artery or perirenal haematonia is well recognised but is rare after ureteric injury. Boston and Smyth (1975) reported hypertension in a 9-year-old girl with bilateral avulsion and anuria but did not discuss the aetiology. Schroeder and Correa (1966) described hypertension in a 17-year-old boy with a calyceal rupture and pararenal pseudocyst; they suggested direct pressure on the kidney as the cause.

Hypertension is not uncommon in association with a large hydronephrotic kidney but may be reversible following its relief. There is clear evidence in our case that relief of the tension in the obstructive hydronephrosis-pseudocyst system both by tapping on 2 occasions and ultimately by reconstructive surgery led to resolution of the hypertension. In this case the degree of hydronephrotic distension was relatively small—it seems likely that it was in fact extrarenal pressure from the large pararenal pseudocyst which, by stretching the renal vessels, reduced the blood flow to the kidney, the resulting ischaemia causing renal hypertension.

Summary

A further case of traumatic avulsion of the upper ureter is described; it was complicated by hypertension and treated by removal of the pseudocyst.

Delay in diagnosis should not be a contraindication to reconstructive surgery which should always be attempted if the kidney is functioning.

The possibility of renal artery ischaemia should be considered when hypertension develops in the presence of a pseduocyst.

References

BARTLEY, O., EKDAHL, P. H. and WAHLQVIST, L. (1966). Rupture of the ureter with pseudocyst formation. *Acta Chirurgica Scandinavica*, **132**, 390-396.

BOSTON, V. E. and SMYTH, B. T. (1975). Bilateral pelvi-ureteric avulsion following closed trauma. *British Journal of Urology*, **47**, 149-151.

DEL VILLAR, R. G., IRELAND, G. W. and CASS, A. S. (1972). Ureteral injury owing to external trauma. *Journal of Urology*, **107**, 29-30.

DIOKNO, A. C. (1974). Avulsion of the proximal ureter secondary to blunt injury. *Journal of Urology*, **111**, 412-414.

JOHNSON, J. M., CHERNOV, M. S., CLOUD, D. T., LINKNER, L. M., DORMAN, G. W. and TRUMP, D. S. (1972). Bilateral ureteral avulsion. *Journal of Paediatric Surgery*, **7**, 723.

KHONSARI, H., MOREHOUSE, D. D. and MACKINNON, K. J. (1971). Pararenal pseudocysts. *British Journal of Urology*, **43**, 164-169.

MORRIS, H. (1908). Hunterian Lectures.

RAO, C. R. (1973). Ureteral avulsion secondary to blunt abdominal injury. *Journal of Urology*, **110**, 188-190.

REZNICHECK, R. C., BROSMAN, S. A. and RHODES, D. B. (1973). Ureteral avulsion from blunt trauma. *Journal of Urology*, **109**, 812-816.

ROE, T. N. (1969). Traumatic rupture of the ureter at the pelvi-ureteric junction in a congenital hydronephrotic kidney. *Medical Journal of Malaya*, **23**, 203-207.

SCHROEDER, K. F. and CORREA, R. J. (1966). Hypertension resulting from an unusual pararenal pseudocyst. *Journal of Urology*, **96**, 119-121.

WILENIUS, R., (1950). Subcutaneous rupture of the ureter. *Annales Chirurgiae et Gynaecologia Fenniae*, **39**, 1-15.

The Authors

B. F. Ribeiro, FRCS, Visiting Lecturer (now Surgical Registrar, The Middlesex Hospital).
J. K. M. Quartey, Professor of Urology.

Requests for reprints to: B. F. Ribeiro, Department of Surgical Studies, The Middlesex Hospital, London W1N 8AA.

British Journal of Urology (1976), **48**, 111-117 ©

Influence of Vesico-ureteral Reflux on the Response to Treatment of Urinary Tract Infections in Female Children

WILLIAM R. FAIR and DUNCAN E. GOVAN

Department of Surgery (Urology), Stanford University School of Medicine, Stanford, California

The purpose of this article is to present data on 3 groups of female children, comprising a total of 169 patients, who were followed through successive episodes of urinary tract infection (UTI) with respect to recurrence of infection. Specifically, the authors will consider: (*a*) the influence of vesico-ureteral reflux on the recurrence rate of infection and (*b*) whether or not surgical correction of reflux influenced the rate of infection.

Materials and Methods

A total of 169 patients followed at Stanford University Medical Centre constitutes the basis of the study. All patients had intravenous pyelograms and voiding cysto-urethrograms performed and were personally followed by one of the authors. Most of the children were white and of middle class socio-economic background. The diagnosis of infection was based, in all instances, on the results of the urine cultures. The criteria for considering a urine culture positive have been outlined in detail previously (Govan and Palmer, 1969).

E. coli was the most common urinary tract pathogen recovered and was responsible for approximately 70% of all infections. No serotyping was done, so it was not possible to differentiate between relapse and reinfection in these patients.

Group A consisted of 66 patients with no evidence of vesico-ureteral reflux. Group B was composed of 42 patients with demonstrated vesico-ureteral reflux, in whom urinary tract infections were treated with medical therapy alone and in whom the reflux was not corrected. Group C comprised 61 patients, all of whom had successful surgical correction of reflux. Only those children presenting with UTI with or without vesico-ureteral reflux, who were free of other congenital urologic or neurologic abnormalities and who were personally followed by one of the authors for at least 1 year, were selected for this study. Of the 169 children presented here, 62 (31 in Group A and 31 in Group C) have been reported on in a previous publication from this institution (Govan and Palmer, 1969).

Treatment Modalities. None of the infections were treated with any long-term suppressive medication. However, those patients who had surgical correction of reflux were prescribed an appropriate antimicrobial agent (*vide infra*) postoperatively for a period of 4 to 6 weeks only. In all other cases treatment of a documented infection consisted of 10 days of a specific antibacterial agent following diagnosis by urine culture. A patient was considered free of infection following treatment only if a sterile urine culture was obtained 3-4 days after the cessation of all antibiotics. A variety of antibacterial agents were used; generally the choice was made on the basis of bacterial sensitivity results. The primary antibacterial drugs used for therapy were sulfisoxazole, penicillin-G, and nitrofurantoin.

Of the 66 children without vesico-ureteral reflux, who were followed through at least one and in some instances as many as 11 episodes of infection, the follow-up time averaged 40 months.

Table I

Grade of Ureterovesical Reflux

	Group B (42 patients), medication, no surgery	Group C (61 patients), surgery plus medication
No. of ureters	66	105
Grade I	26	12
Grade II	35	46
Grade III	5	47

In the groups of children presenting with reflux, those treated conservatively with medication alone (Group B) and those whose reflux was corrected by surgery (Group C), both were followed for a minimum of 12 months.

Decision for Surgical Correction. Those children, in whom adequate control of UTI's was not obtained with medical therapy only, underwent surgical correction of reflux. In general, "adequate control" indicates that the patient had persistently sterile urine or was experiencing infrequent episodes of minimally symptomatic bladder infections or asymptomatic bacteriuria.

Grading of Reflux. The degree of reflux was graded as previously described (Filly *et al.*, 1974). The severity of reflux varied in the 2 groups of children presenting with vesico-ureteral reflux. As seen in Table I, some children had only unilateral reflux; thus, Group B represents 42 children with a total of 66 refluxing ureters. Group C comprised 61 patients with a total of 105 refluxing ureters. In general, those children undergoing surgery had more severe degrees of reflux.

Originally the Hutch techniques of ureteroneocystostomy were employed (Hutch, 1963; Hutch, Smith and Osborne, 1968). Because of the high incidence of persistent reflux associated with those procedures, we later adopted the Politano-Leadbetter approach as our primary surgical technique. The majority of the patients had a variation of this original technique in that the ureter was exposed from outside the bladder as well as circling the orifice from within. The ureter was then reanastomosed under direct vision, using the tunnelling procedures advocated by the above authors (Politano and Leadbetter, 1958). If the ureter was severely dilated the distal one-third of the ureter was tapered prior to reimplantation into the bladder.

All of the children in Group C had successful correction of vesico-ureteral reflux.

Results

The results will be considered under the following 3 groups:

Group A: Those girls who had no evidence of vesico-ureteral reflux: 66 patients.
Group B: Girls having vesico-ureteral reflux treated with medical therapy only: 42 children.
Group C: Patients having vesico-ureteral reflux corrected by surgery, plus medical therapy: 61 children.

Children without Reflux (Group A)

The 66 patients were followed through as many as 11 episodes of urinary tract infections, each treated with a short course of a specific antibacterial agent (Table II). The mean time of observation in the entire group was 40 months with all patients followed for at least 12 months. Table II

Table II

Results of Short-term Treatment in Female Children without vesico-ureteral Reflux (Group A)

Treatment number	Patients at start	Patients cured*	Patients with recurrent infections	Percentage with recurrences
1	66	16	50	75
2	50	4	46	70
3	46	9	37	56
4	37	7	30	49
5	30	6	24	39
6	24	6	18	30
7	18	4	14	23
8	14	4	10	16
9	10	1	9	15
10	9	1	8	13
11	8	3	5	8

* No further infections during observation period (mean = 40 months).

indicates exactly what happened in terms of reinfection when these children were treated for a specific infection and urine cultures confirmed that the treatment was indeed successful. Thus, of the 66 patients (100%) who were treated for one infection, 50 (75%) went on to develop a second infection at some time during the follow-up period. After treatment of this second infection 4 additional patients were "cured" and had no further infections during the period of observation, while the majority went on to experience an additional infection. The same tendency occurred following treatment of subsequent infections. Thus, more than one-half of the girls in the study had only 3 or 4 infections and did not have a positive culture during the remainder of the follow-up period. In general, of those patients treated for any given infection, approximately 20% were "cured" each time and did not experience another infection. However, 80% of those given this short-term treatment with a specific antibacterial agent went on to develop another infection. This was true whether it was the patient's first or subsequent infection.

Children with Reflux treated with Medical Therapy only (Group B)

In comparing patients with vesico-ureteral reflux treated with medical and surgical modalities (Group B versus Group C) it is important to consider first the rate of infection prior to referral to Stanford. Both groups of children averaged slightly more than 2 infections per year during this time. Hence, there was no significant difference in the incidence of infection prior to entry into the study. Also, about 50% of the infection episodes in each group were clinically diagnosed as pyelonephritis (fever, with or without chills and back or abdominal pain). Those children with recurrent severe episodes of pyelonephritis, particularly if accompanied by pyelographic changes consistent with this diagnosis and who were not kept sterile with antibacterial medication, were operated upon for correction of the reflux and, hence, were included in Group C. Thus, it appeared that the groups were quite comparable in regard to both the incidence and type of infection prior to entering the study, although those in Group C were more likely to have had recurrent pyelonephritis not readily controlled by medication.

The Figure indicates the percentage of patients who were "cured" following each treatment episode in these 42 female children (Group B) with demonstrated vesico-ureteral reflux who

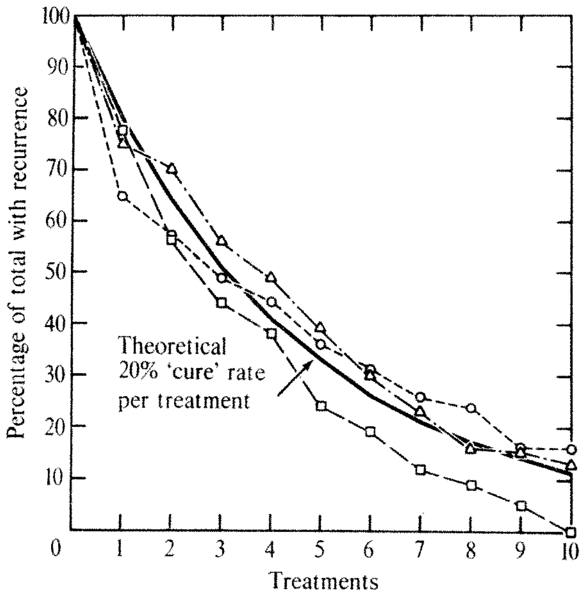


Fig. The recurrence rate of new infection for the 3 groups of children following each successful treatment is plotted against the theoretical 20% "cure" rate per treatment (black line).

were followed for at least 1 year after the demonstration of reflux and in whom surgery was not performed. As with Group A children, 20 to 25% of those treated for a specific infection did not develop another infection but maintained sterile urine throughout the follow-up period. The Figure also indicates that the 2 patient populations showed a similar response to treatment whether it was the first infection or a subsequent infection.

Children with Vesico-Ureteral Reflux treated surgically

Group C consisted of 61 patients followed for at least 12 months after the correction of the reflux. As indicated in the Figure these patients had a very similar postoperative infection rate when compared with the patients without reflux (Group A) and those children in whom the reflux was not surgically corrected (Group B). That is, approximately 20% of the patients were cured with each course of short-term medical therapy. An important observation in both groups of refluxing children (B and C) was that the incidence of clinical pyelonephritis was approximately 50% of all infections in both Groups B and C prior to referral. This was reduced to 10% of the total number of infections in those surgically treated (Group C) and less than 20% of the infections in those medically treated (Group B). The differences are not statistically significant but indicated a marked decrease in symptomatic pyelonephritis in both populations compared with the rate prior to the initiation of close medical and/or surgical supervision.

The children in Groups B and C were not arbitrarily assigned to either a medically or surgically-treated group. In general, the non-surgical group was comprised of children with lesser degrees of reflux than those children who were treated operatively (Table I). Also, those children whose infections could not be adequately controlled with close medical supervision were considered as surgical candidates. The 2 groups, therefore, are not strictly comparable in the severity of the reflux prior to entering into our study.

Comparison of the Results

As shown in the Figure, the results of treatment of infection were essentially the same. In the children without reflux, and in those whose reflux was surgically corrected, the percentage experiencing recurrent infections following each episode of treatment paralleled the theoretical 20% "cure" rate. Thus, there appears to be no difference in the recurrence rate of infections in those children with reflux corrected surgically and those treated medically. More importantly, the recurrence rate in both of these groups does not differ significantly from the group of children with UTI's who do not have ureterovesical reflux.

Comments

There were several interesting observations apparent during the course of these studies. All patients on the study received 10 days of a specific antibacterial agent at the time the infection was diagnosed; no long-term suppressive medication was given to this group. As shown in the Figure our results in the group of children without reflux confirmed the earlier results of Kunin (1970) which indicate, essentially, that each time we treat a group of children presenting with UTI's, 20% of the patients will have no further infection but that 80% will develop another infection. If the remaining 80% who develop another infection are again treated and sterilised, another 20% of this population will be "cured" but 80% of this group will still go on to develop a further infection.

Prior to referral to our institution over 50% of the infections in the patients comprising both Group B and Group C were associated with fever, with or without flank pain, symptoms clinically suggestive of pyelonephritis (Govan *et al.*, 1974). This is quite in contrast to the benign type of clinical infection experienced in the children of Group A (Fair *et al.*, 1974) in whom a diagnosis of pyelonephritis was suspected in fewer than 10% of the total number of infections.

It should be noted that Groups B and C were not strictly comparable, in that there was a marked difference in the degree of reflux found in the patients comprising the 2 groups. However, the overall infection rate was similar in both populations under the same type of medical management.

Of particular interest is the observation that the incidence of clinical pyelonephritis was reduced to less than 20% of all infections in both groups. This compares favourably with an incidence of clinical pyelonephritis of less than 10% of all infections in non-refluxing children (Group A) and is in agreement with other studies in similar patient populations (Winberg, Larson and Bergström, 1970). Winberg *et al.* (1970) found that in children with reflux, whose infections were under bacteriological control, the incidence of clinical pyelonephritis was similar to that occurring in children without reflux. In addition to the similarities between the 2 groups of patients with reflux as to the type and incidence of infection prior to entry into the study, it is also of note to compare the "cure" rate of these children with each successful treatment. As shown in the Figure both groups had about 20% of the children "cured" following each course of treatment, whether the reflux was surgically corrected or not. Quite significantly, the "cure" rate was similar for the 3 groups of children with or without reflux and did not differ in those children with reflux corrected by surgery plus medication and those treated with medication alone. All 3 groups paralleled the theoretical 20% "cure" rate previously described by Kunin (1970).

At this point it is perhaps important to realise in discussing a prevention of recurrences, we are, for the most part, talking about preventing *reinfection* rather than *relapse* of an improperly-treated infection. Kunin and Halmagyi (1962) and Bergström *et al.* (1967) have shown that 85% of urinary tract infections are new infections caused by a different organism each time. Thus it becomes clear that long periods of treatment are simply preventing reinfections and not eradicating relapses due to inadequate treatment.

In summary, from these data one may draw the following conclusions:
1. Urinary tract infections are not totally prevented by correction of vesico-ureteral reflux; 2. The rate of reinfections in surgically-treated *versus* medically-treated children with reflux is similar; 3. The "cure" rate is similar, when one compares the 2 groups of children with reflux (Groups B and C), with the children without vesico-ureteral reflux (Group A).

From a prospective point of view it becomes apparent that it would be most helpful to identify those girls who are likely to develop multiple recurrences and treat those children prophylactically with long-term suppressive therapy. The results of this study, which confirms the earlier work of Kunin (1970), show that medication alone will produce a long-term cure in 20% of young white females whether it is the first infection or a subsequent infection. Use of long-term suppressive medication such as advocated by Normand and Smellie (1965) gave excellent results in a group of children without reflux similar to ours. The fact that this approach to the problem has been shown to be effective underscores the major problem in treating these children; that is, identifying those girls who are most susceptible to recurrent infections and directing long-term therapy to that group. Since more than 50% of the children will have no more than 3 or 4 infections, we suggest that in those female children whose reflux is not deemed serious enough to warrant surgery (Govan *et al.*, 1974) or who continue to have reinfections following surgery, as well as in those children who do not have vesicoureteral reflux at all, it would be appropriate to begin these patients on long-term suppressive medication after the third or fourth infection in an effort to select those children who are most likely to benefit from this form of therapy.

Our current practice in such instances of recurrent bacteriuria is initially to sterilise the child with appropriate medication for 10 days and then to place the child immediately on a low dose of nitrofurantoin (usually in the form of Macrodantin 25 or 50 mg) given just before bedtime. This medication is prescribed for 6 months, then discontinued. Should the child develop a further infection, then the whole procedure is repeated. This regimen has been highly successful in lowering the frequency and morbidity of infections in this small, but difficult population.

Summary

3 groups of female children, comprising a total of 169 patients, were followed through successive episodes of urinary tract infection with respect to recurrence of infection.

Group A consisted of 66 patients with no evidence of vesico-ureteral reflux. Group B comprised 42 patients with demonstrated vesico-ureteral reflux. The infections in these patients were treated with medical therapy alone and the reflux was not corrected. Group C consisted of 61 children who had surgical correction of vesico-ureteral reflux. While Groups B and C were not strictly comparable, the data indicate that there was no demonstrable difference in the rate of urinary tract infection among the 3 groups.

Following short-term specific antibacterial therapy of a new infection, about 20% of children in each group were "cured", *i.e., had no further infections during the 12 months or more that they were subsequently followed by the authors.*

Patients with less severe grades of reflux treated by medication alone (Group B) experienced no greater rate of reinfection than those children presenting with infections in the absence of vesico-ureteral reflux.

In those children whose infections could not be adequately controlled by antimicrobial therapy, and those patients with severe (Grade III) reflux, surgery was performed to eliminate the vesico-ureteral reflux.

The data also reinforced the concept that correction of reflux does not eliminate the need for constant vigilance and proper treatment of recurrent infections even after successful surgery has been carried out.

References

BERGSTRÖM, T., LINCOLN, K., ØRSKOV, F., ØRSKOV, I. and WINBERG, J. (1967). Studies of urinary tract infections in infancy and childhood. VIII. Reinfection *vs.* relapse in recurrent urinary infections. Evaluation by means of identification of infecting organisms. *Journal of Pediatrics*, **71**, 13-20.

FAIR, W. R., GOVAN, D. E., FRIEDLAND, G. W. and FILLY, R. A. (1974). Urinary tract infections in children. I. The non-refluxing female child. *Western Journal of Medicine*, **121**, 366-373.

FILLY, R., FRIEDLAND, G. W., GOVAN, D. E. and FAIR, W. R. (1974). Urinary tract infections in children. II. Roentgenologic aspects. *Western Journal of Medicine*, **121**, 374-381.

GOVAN, D. E., FAIR, W. R., FRIEDLAND, G. W. and FILLY, R. A. (1974). Urinary tract infections in children. III. The refluxing female child. *Western Journal of Medicine*, **121**, 382-389.

GOVAN, D. E. and PALMER, J. M. (1969). Urinary tract infection in children—the influence to successful antireflux operations in morbidity from infection. *Pediatrics*, **44**, 677-684.

HUTCH, J. A. (1963). Ureteric advancement operation: anatomy, technique and early results. *Journal of Urology*, **89**, 180-184.

HUTCH, J. A., SMITH, D. R. and OSBORNE, R. (1968). Review of a series of ureterovesiculoplasties. *Journal of Urology*, **100**, 285-289.

KUNIN, C. M. (1970). The natural history of recurrent bacteriuria in school girls. In *Renal Infection and Renal Scarring*, ed. by P. Kincaid-Smith. Melbourne: Mercedes Publishing Services, pp. 3-23.

KUNIN, C. M. (1970). The natural history of recurrent bacteriuria in school girls. *New England Journal of Medicine*, **282**, 1443-1448.

KUNIN, C. M. and HALMAGYI, N. E. (1962). Urinary-tract infections in school children. II. Characterization of invading organisms. *New England Journal of Medicine*, **266**, 1297-1301.

NORMAND, I. C. S. and SMELLIE, J. M. (1965). Prolonged maintenance chemotherapy in the management of urinary infections in childhood. *British Medical Journal*, **I**, 1023-1026.

POLITANO, V. A. and LEADBETTER, W. F. (1958). An operative technique for the correction of vesicoureteral reflux. *Journal of Urology*, **79**, 932-941.

WINBERG, J., LARSON, H. and BERGSTRÖM, T. (1970). Comparison of the natural history of urinary infection in children with or without vesicoureteric reflux. In *Renal Infection and Renal Scarring*, ed. by P. Kincaid-Smith. Melbourne: Mercedes Publishing Services, pp. 293-302.

The Authors

William R. Fair, MD, Associate Professor of Surgery (now Professor of Surgery, Division of Genitourinary Surgery, Washington University School of Medicine). Recipient of Research Career Development Award No. EI70107, National Institute of Allergy and Infectious Diseases, National Institutes of Health, U.S.P.H.S.

Duncan E. Govan, MD, Phd, Professor of Surgery, Division of Urology, Stanford School of Medicine.

British Journal of Urology (1976), **48**, 118 ©

Short Case Report

Bilateral Renal Carcinomas Treated Operatively

Bilateral renal tumours are very rare. Even rarer are the cases of such tumours treated operatively.

Case History

Female, Z. K., aged 70, was admitted in March 1975 with gross haematuria. Previously, in August 1954, I had done a left nephrectomy for renal cell carcinoma; postoperatively she was treated with radiotherapy.

Physical examination on this admission revealed a large palpable right kidney. Intravenous pyelogram and angiogram showed tumour of the upper pole of the right solitary kidney (Fig. 1), which was treated by resection of the upper pole. The patient left the hospital 1 month after the operation: blood urea 46 mg/100 ml, creatinine 1·4 mg/100 ml. Intravenous pyelography (Fig. 2) revealed good function of the kidney. Histology—renal cell carcinoma.

Comment

Between appearance of the first and the second tumours 20 years elapsed. The problem is whether the tumour of the right kidney was metastatic after left nephrectomy or quite a new one. Another interesting aspect is the fact that the patient happened to be operated on by the same surgeon in the cases of both tumours.

Borski and Kimbrough (1954) described a case of bilateral carcinoma in polycystic renal disease. Grabstald and Avilles (1968) compiled from the literature 45 renal cell cancers in solitary kidneys, among them 5 of their own cases. All the authors agree that the only effective treatment of a tumour of a solitary kidney is operative. Enthusiasts of extracorporeal renal surgery hope that bench surgery may create new opportunities for similar cases (Wickham, 1975).

Stefan Wesolowski

Department of Urology, Medical Academy, Oczki 6, Warsaw, Poland

References

Borski, A. A. and Kimbrough, J. C. (1954). Bilateral carcinoma in polycystic renal disease—a unique case. *Journal of Urology*, **71**, 677-681.

Grabstald, H. and Avilles, E. (1968). Renal cell cancer in the solitary or sole-functioning kidney. *Cancer*, **22**, 973-987.

Wickham, J. E. A. (1975). Conservative renal surgery for adenocarcinoma: the place of bench surgery. *British Journal of Urology*, **47**, 25-36.

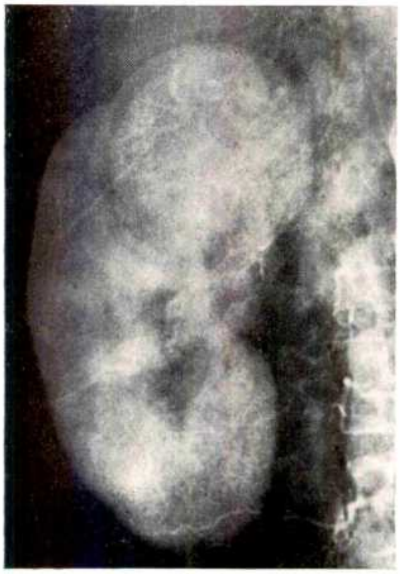


Fig. 1

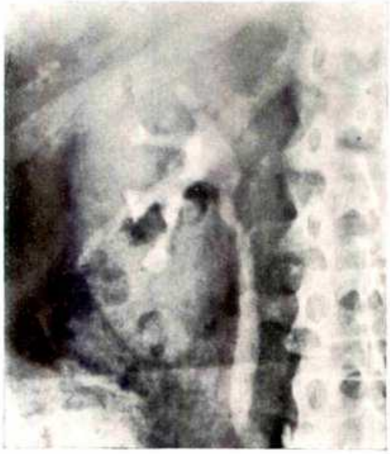


Fig. 2

British Journal of Urology (1976), 48, 119-121 ©

Percutaneous Suprapubic Cystostomy after Spinal Cord Injury

J. B. COOK and P. H. SMITH
Yorkshire Regional Spinal Injuries Unit, Pinderfields General Hospital, Wakefield

Suprapubic cystostomy was, for many years, the treatment of choice in the management of prostatic hypertrophy with retention of urine; for many patients it was the only treatment. Its use in patients following spinal cord injury was discussed by Thomson Walker (1917) and by Vellacott and Webb-Johnson (1919).

The formal cystostomy had many disadvantages but these were largely overcome by the Riches technique (1943). Gradually, however, with the advent of latex catheters and antibiotic therapy the technique of intermittent catheterisation (Guttmann and Frankel, 1966) became more fashionable. It is, however, time-consuming and satisfactory only in those units with numbers of well-trained medical and nursing staff.

The introduction of the Bard suprapubic catheter (the suprapubic angiocath, 1966, S. P. Bard-Davol Ltd) allowed us to reconsider the virtues of percutaneous suprapubic catheterisation (Smith, Cook and Robertson, 1969) in the hope that its use would save nursing and medical time and that the preservation of the integrity of the urethra would minimise both infective complications and the possibility of external sphincter spasm. We report our results in our first 43 patients treated with either the Bard catheter or with a Braun peritoneal dialysis catheter which is somewhat more rigid and has proved more reliable.

Method

Suprapubic cannulae were inserted into adult male paraplegic patients at the time of admission to the Spinal Injuries Unit after allowing the bladder to distend so that it was palpable. The cannula was inserted half-way between the umbilicus and the symphysis in the midline and angled at 45° to the vertical as suggested by Riches (1943). The procedure was carried out by a member of the medical staff and the bladder allowed to drain freely into a drainage bag whilst the patient was immobilised in bed. Any cannula which blocked or became displaced was replaced when the bladder filled. This has presented no difficulty. If satisfactory micturition had not been established by the time of mobilisation the cannula was removed and an intermittent catheterisation regime adopted because the patients commonly found the cannula inconvenient when mobilised.

Smith, Cook and Robertson (1969) reported the use of the Bard supracath for suprapubic drainage of the paralysed bladder in 12 patients who had not previously been catheterised. Of the 12 patients, 6 maintained sterile urine throughout the course of suprapubic catheterisation, 1 for as long as 30 days. This method was used in a further 6 patients but there was difficulty because of mechanical blockage of the catheter by kinking. It was decided to continue suprapubic drainage using a more rigid but equally fine (9 Charriere) catheter. The Braun peritoneal dialysis catheter (distributed by Armour Pharmaceuticals Ltd) was chosen.

The method was used only in male paraplegics, some having had previous urethral catheterisation. Antibiotics and urinary antiseptics were not used until clinical urinary infection had

Table I

Duration of Suprapubic Drainage and Life of each Catheter

	Type of catheter		
	Supracath	Dialysis	Both
Patients	18	23	41
Duration of suprapubic drainage (average—days)	24	57	45
Life of each catheter (average—days)	11	26	–

Table II

Urine Infection after Suprapubic Drainage

	Type of catheter		
	Supracath	Dialysis	Total
Patients	18	23	41
Urine sterile throughout	9 (50%)	10 (43%)	19 (46%)
Duration (average—days)	18	49	38
Urine infected	9 (50%)	13 (57%)	22 (54%)
Onset of infection (average—days)	33	27	30

supervened and no instillation was made into the bladder. The urine was scanned bacteriologically at weekly intervals. A significant infection was taken to be either more than 10^5 organisms per ml or 5 cells per high-power field and a positive culture. Bladder emptying was checked by aspiration with a syringe and by 2-film intravenous urograms done at weekly intervals.

Results

The results are shown in Tables I and II. It was found (Table I) that the average life of the peritoneal dialysis catheter was 26 days as compared with 11 days for the Bard supracath. Using the dialysis catheter, it was possible to maintain suprapubic drainage for an average of 8 weeks with a range from 4 to 19 weeks.

The proportion of patients maintaining sterile urine throughout the period of suprapubic drainage (Table II) was marginally less with the more rigid (peritoneal) catheter, 43% as compared with 50% with the supracath. However, when the duration of suprapubic drainage was taken into account, it was clear that the peritoneal dialysis catheter was a considerable advance in that it was possible to maintain sterility for an average of 7 weeks without antibiotics or urinary antiseptics.

Those patients who developed infected urine during the course of suprapubic drainage (Table II) included some who had previous urethral catheterisation, 1 with a urethral fistula and a number whose suprapubic catheter had been manipulated for bladder pressure recording. Of those whose urine was sterile at the time of first suprapubic catheterisation, but who later developed infection, it was possible to maintain sterility for an average of 4 weeks.

Discussion

The results of suprapubic drainage of the paralysed bladder by means of a fine catheter in 41 male paraplegic patients are encouraging. The initial problem of blockage by mechanical kinking of the catheter has been greatly reduced by the use of a stronger peritoneal dialysis catheter. More than 40% of patients maintained a sterile urine for an average of 7 weeks without the use of antibiotics or urinary antiseptics. It is difficult to compare these results with those of intermittent catheterisation since the criterion usually quoted with reference to intermittent catheterisation is the state of the urine on discharge from hospital, when a variety of treatments may have been given subsequent to intermittent catheterisation.

Summary

The results of treatment of urinary bladder paralysis with small calibre (9 Charriere) suprapubic drainage in 41 male patients are described. It was found that suprapubic drainage could be maintained for an average of 8 weeks and that the urine in 43% of patients remained sterile for an average of 7 weeks. This technique merits further trial, both in the paraplegic patient and in normal patients requiring catheterisation because of obstruction of the lower urinary tract.

References

GUTTMANN, L. and FRANKEL, H. (1966). The value of intermittent catheterisation in the early management of traumatic paraplegia and tetraplegia. *Paraplegia*, **4**, 63-84.

RICHES, E. W. (1943). The methods and results of treatment in cases of paralysis of the bladder following spinal injury. *British Journal of Surgery*, **31**, 135-147.

SMITH, P. H., COOK, J. B. and ROBERTSON, W. G. (1969). Stone formation in paraplegia. *Paraplegia*, **7**, 77-85.

THOMPSON WALKER, J. W. (1917). The bladder in gunshot and other injuries of the spinal cord. *Lancet*, **1**, 173-179.

VELLACOTT, P. N. and WEBB-JOHNSON, A. E. (1919). Spinal injury with retention of urine, the avoidance of catheterisation. *Lancet*, **1**, 733-737.

The Authors

J. B. Cook, MD, FRCP, Consultant in Neurology.
P. H. Smith, FRCS, Consultant in Urology.

British Journal of Urology (1976), **48**, 122 ©

Short Case Report

Lymphocele following Renal Transplantation: an Unusual Cause of Urinary Retention

Retroperitoneal pelvic lymphoceles have been reported in 1% to 2% of patients receiving renal transplants (Starzi *et al.*, 1970; Schweizer *et al.*, 1972). They usually become evident within 3 months following transplantation and are thought to be due to disruption of the small lymphatics adherent to the iliac vessels. Their most common mode of presentation has been mild deterioration of renal function caused by ureteric obstruction.

Case Report

A 36-year-old man had been on chronic haemodialysis for 4 months when he received a renal transplant from a cadaveric donor. There was an immediate diuresis and, within 10 days following surgery, renal function returned to normal. The patient was discharged 18 days after transplantation, voiding normally, with a serum creatinine of 1·7 mg%. He was readmitted 1 month later in urinary retention, after several days of progressive voiding dysfunction. Intravenous pyelography (Fig.) demonstrated prompt function of the graft despite moderate ureteric obstruction and a large left paravesical mass displacing the bladder to the right. Retrograde cysto-urethrogram confirmed the presence of the paravesical mass and revealed an intrinsically normal urethra and bladder neck. At exploration a large pelvic lymphocele was evacuated and drained, resulting in immediate relief of all voiding symptoms and restoration of the normal configuration of the lower urinary tract.

Comment

The patient reported herein represents, to our knowledge, the first report of bladder outlet obstruction due to post-transplantation lymphocele formation. This complication, 2 months following surgery, was due to compression and distortion of the vesical neck by the expanding lymphocele. Disruption and drainage of peri-iliac lymphatic channels following dissection in the region has been well demonstrated radiographically (Madura, Dunbar and Cerilli, 1970). These channels probably heal and recanalise readily; therefore, temporary drainage is the only treatment required.

MARTIN SCHIFF, JR. and ROBERT A. FELDMAN

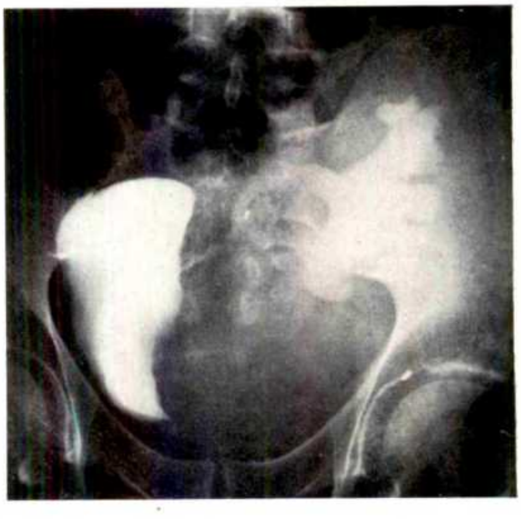
Section of Urology, Department of Surgery, Yale University School of Medicine, New Haven, Connecticut, 06504

References

MADURA, J. A., DUNBAR, J. D. and CERILLI, G. J. (1970). Perirenal lymphocele as a complication of renal homotransplantation. *Surgery*, **68**, 310-313.

SCHWEIZER, R. T., CHO, S., KOUNTZ, S. L. and BELZER, F. O. (1972). Lymphoceles following renal transplantation. *Archives of Surgery*, **104**, 42-45.

STARZL, T. E., GROTH, C. G., PUTNAM, C. W., *et al.* (1970). Urological complications in 216 human recipients of renal transplants. *Annals of Surgery*, **172**, 1-22.



British Journal of Urology (1976), **48**, 123-126 ©

Asymptomatic Phaeochromocytoma of the Bladder Co-existing with Carcinoma

C. H. LEONG, K. K. WONG and D. SAW

Department of Surgery, University of Hong Kong, Queen Mary Hospital, Hong Kong and The Institute of Pathology, Medical and Health Department, Hong Kong

Phaeochromocytomata characteristically occur in the adrenals. Extra-adrenal sites have also been reported in 10% of cases (Fries and Chamberlin, 1968; Remine *et al.*, 1974; Van Way *et al.*, 1974).

The urinary bladder is one of the possible extra-adrenal sites. The first report of a phaeochromocytoma of the urinary bladder was made by Zimmerman *et al.* (1953). Since then 35 other cases have been reported in the literature (Sarma, 1969; Albores-Saavedra *et al.*, 1969; Cummins, Hill and Williams, 1969; Silver *et al.*, 1971; Bogaert and Vermeulen, 1972; Doctor, Phadke and Sirsat, 1972; Remine *et al.*, 1974).

We report one further case of phaeochromocytoma of the urinary bladder, with the exceptional features of:

(*a*) Absence of symptoms connected with phaeochromocytoma;
(*b*) Association with bladder carcinoma.

Case Report

A 63-year-old Chinese male, L. C. K., Hospital No. QM40936/74, was admitted into the University Department of Surgery because of haematuria for 2 months. This was associated with dysuria and frequency of micturition. His past health was good and there was no history of hypertension. Examination on admission revealed his blood pressure to be 130/80 mm Hg. Urological examination was negative, save for an enlarged prostate. Emergency cystoscopy was done under local anaesthesia and this showed a tumour on the right lateral wall of the bladder obliterating the right ureteric orifice. Biopsy was taken and showed histological evidence of transitional cell carcinoma Grade I (W.H.O. classification). Meanwhile his daily blood pressure reading remained normal. An examination under anaesthesia was carried out and the clinical impression was that there was muscular invasion but it was still resectable. Radical cystoprostatectomy with pelvic block dissection was done. The postoperative course was uneventful except for some minor wound infection.

Gross appearance of the specimen revealed a large, papillary growth measuring 7·5 cm across and 3·5 cm in height. Its cut surface showed friable, greyish-white tumour tissue supported by a pedicle 6 × 7 mm, attached to the posterior wall. About 1·5 cm away from the base of the pedicle there was a well-circumscribed nodule 10 × 8 mm situated just beneath the mucosa and within the muscle coat (Fig. 1). It turned mahogany brown after fixation in 4% formaldehyde.

Microscopic sections revealed an endophytic pattern of papillary growth. There were solid strands and masses of fairly compact transitional epithelium separated by delicate stroma (Fig. 2). Towards the centre the tumour cells arranged in sheets with indistinct cell outline. Their nuclei were small, vesicular and exhibiting mild to moderate pleomorphism. In many the nucleoli were distinct. Mitosis varied from 0-1 per high-power field. There was no invasion into the pedicle or the base.

Sections of the brownish nodule, however, revealed masses of tumour cells which at places were separated by thin fibrous septa into ill-defined alveolar groups. The tumour cells contained abundant, granular cytoplasm which had a bluish-grey appearance with haematoxylin and eosin. Their nuclei were uniform, slightly vesicular with fine chromatin clumping. In other areas both granular and highly vacuolated tumour cells were present, the latter with crescentic nuclei located along the periphery (Fig. 3). The edge of the tumour was well demarcated from the adjacent bundles of smooth muscle. This is the picture of a phaeochromocytoma.

Retrospective review of this patient's case history failed to elicit any clinical features to suggest a functionally active phaeochromocytoma. Surprising enough, the systolic blood pressure remained stable in the region of 120 mm Hg throughout the operation when the bladder was repeatedly manipulated.

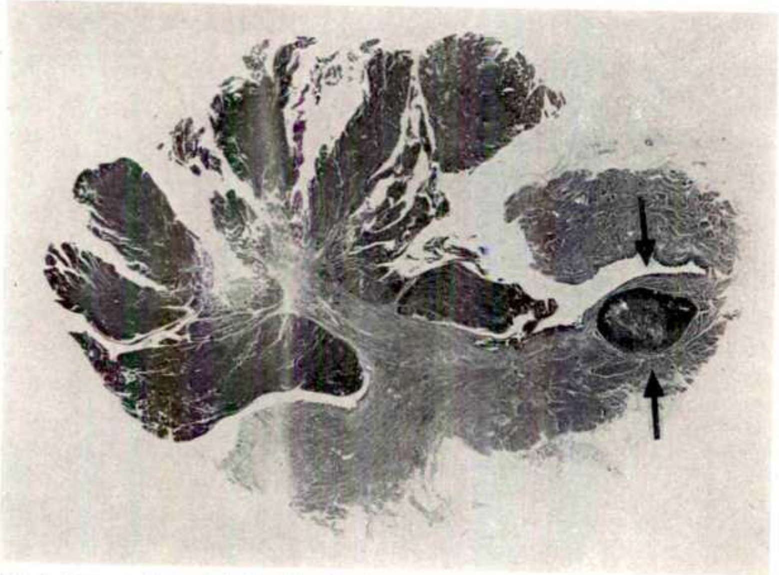


Fig. 1. Large section of the bladder showing both the papillary carcinoma and phaeochromocytoma (indicated by arrows). H and E. × 1.

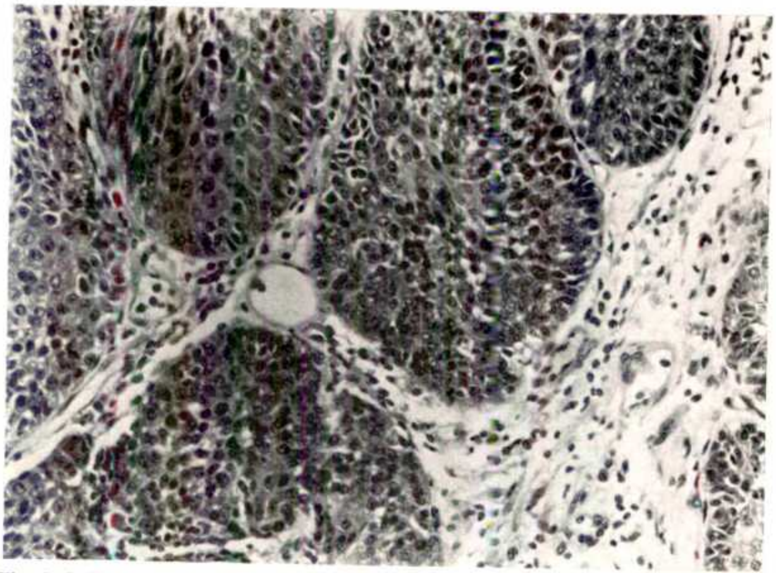


Fig. 2. Solid masses of transitional carcinoma showing clear cell outline with nuclei which are regularly arranged and uniform looking. These are separated by loose, scanty stroma. H and E. × 215.

Discussion

Phaeochromocytomata are usually associated with either sustained or paroxysmal attacks of severe hypertension. When they occur in the bladder they exhibit a peculiar symptom complex by virtue of the fact that they are situated in a structure that changes dimensions constantly. Paroxysmal hypertension commonly occurs in the early hours of the morning when the bladder

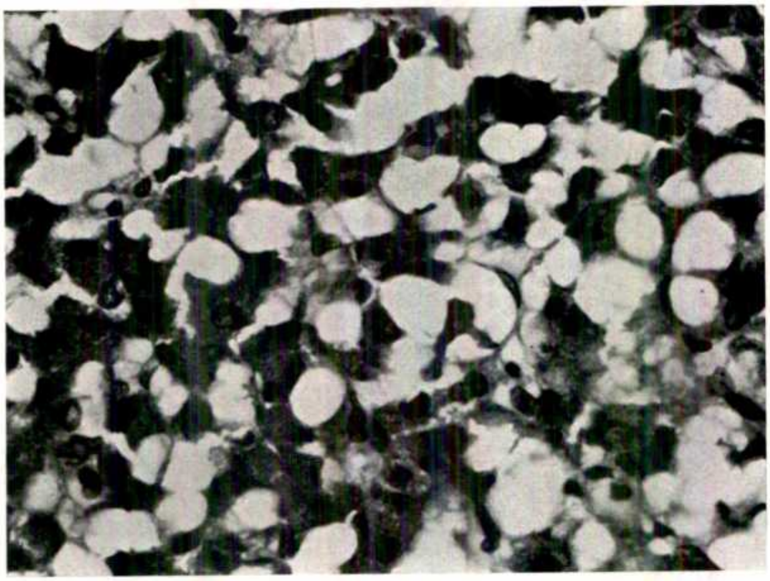


Fig. 3. Another field showing a mixture of tumour cells with abundant granular cytoplasms and those with marked cytoplasm vacuolation. H and E. ×510.

is distended. This is associated with anxiety, palpitation, pallor, sweating, precordial distress, cold clammy extremities, nausea and vomiting (Sarma, 1969).

Our present case demonstrated 2 unusual features. Firstly, this patient had no cardiovascular symptoms. Retrospective questioning of the patient failed to reveal any history suggestive of episodes simulating paroxysmal hypertension. Surprisingly, the blood pressure was undisturbed even on manipulation of the bladder and tumour. Secondly, it co-existed with an epithelial tumour of the bladder.

Phaeochromocytoma of the bladder without cardiovascular symptoms are extremely rare. Scott and Eversole (1960) estimated a figure of less than 10%. Actually, on reviewing the literatures only 2 such cases have been reported (Pugh, Gresham and Mullaney, 1960; Withycombe, 1965).

A satisfactory explanation of absence of hypertension has not been found. Sarma (1969) believed that the tumour may consist mainly of the non-chromaffin paraganglioma which are non-secreting. Pugh *et al.* (1960) believed that, though non-secretory, these tumours are potentially secretory and may produce paroxysmal hypertensive complex after a period of dormancy.

Co-existing phaeochromocytomata and epithelial tumour of the bladder have never been described and to the best of our knowledge this is the first case reported in the literature. Such co-existence is definitely possible as paraganglioma tissue which are the precursors of phaeochromocytomata are commonly found in the wall of normal bladders (Zimmerman *et al.*, 1963; Fries and Chamberlin, 1968; Van Way *et al.*, 1974).

The prognosis of bladder phaeochromocytomata in benign cases is good. Cure can be achieved by partial cystectomy with removal of the tumour. Malignant changes have been reported in 3 cases (Pugh *et al.*, 1960; Higgins and Tresidder, 1966; Moloney, Cowdell and Lewis, 1966). In our present case the phaeochromocytoma is benign and the prognosis of the patient will largely depend on the subsequent behaviour of the co-existing transitional cell carcinoma.

Summary

A case of asymptomatic phaeochromocytoma occurring in co-existence with a transitional cell carcinoma of the urinary bladder is reported and the significant characteristics discussed.

We are grateful to Prof. G. B. Ong for his help in preparing this case note.

References

ALBORES-SAAVEDRA, J., MALDONADO, M. E., IBARRA, J. and RODRIGUEZ, H. A. (1969). Pheochromocytoma of the urinary bladder. *Cancer*, **23**, 1110-1118.

BLAIR, D. W. and BRANWOOD, A. W. (1963). Phaeochromocytoma of the urinary bladder. *British Journal of Urology*, **35**, 293-296.

BOGAERT, M. G. and VERMEULEN, A. (1972). Pheochromocytoma of the urinary bladder with inconclusive chemical and pharmacologic tests. *American Journal of Medicine*, **53**, 797-800.

CUMMINS, B. H., HILL, S. and WILLIAMS, J. L. (1969). Phaeochromocytoma of the urinary bladder. *British Journal of Urology*, **41**, 71-74.

DOCTOR, V. M., PHADKE, A. G. and SIRSAT, M. V. (1972). Pheochromocytoma of the urinary bladder. *British Journal of Urology*, **44**, 351-355.

FRIES, J. G. and CHAMBERLIN, J. A. (1968). Extra-adrenal phaeochromocytoma: literature review and report of a cervical pheochromocytoma. *Surgery*, **63**, 268-279.

HIGGINS, P. M. and TRESIDDER, G. C. (1966). Phaeochromocytoma of the urinary bladder. *British Medical Journal*, **2**, 274-277.

MOLONEY, G. E., COWDELL, R. H. and LEWIS, C. L. (1966). Malignant phaeochromocytoma of the bladder. *British Journal of Urology*, **38**, 461-470.

PUGH, R. C. B., GRESHAM, C. A. and MULLANEY, J. (1960). Phaeochromocytoma of the urinary bladder. *Journal of Pathology and Bacteriology*, **79**, 89-107.

REMINE, W. H., CHONG, G. C., VAN HEERDEN, J. A., SHEPS, S. G. and HARRISON, E. G. (1974). Current management of phaeochromocytoma. *Annals of Surgery*, **179**, 740-748.

SARMA, K. P. (1969). *Tumours of the Urinary Bladder*. London: Butterworths.

SCOTT, W. W. and EVERSOLE, S. L. (1960). Pheochromocytoma of the urinary bladder. *Journal of Urology*, **83**, 656-664.

SILVER, J., THOMAS, D., YOUNG, R. and DOWLING, R. H. (1971). Phaeochromocytoma of the bladder. *Proceedings of the Royal Society of Medicine*, **64**, 670-672.

VAN WAY, C. W., SCOTT, H. W., PAGE, D. and RHAMY, R. K. (1974). Pheochromocytoma. In *Current Problems in Surgery*, June. Chicago: Year Book Medical Publishers.

WITHYCOMBE, J. F. R. (1965). Quoted by Higgins and Tresidder.

ZIMMERMAN, I. J., BIRON, R. E. and MACMAHON, H. E. (1953). Phaeochromocytoma of the urinary bladder. *New England Journal of Medicine*, **249**, 25-26.

The Authors

C. H. Leong, FRCS, FRCSE, FACS, Senior Lecturer in Surgery.
K. K. Wong, MB, BS, Medical and Health Officer.
D. Saw, MB, BS, Medical and Health Officer.

British Journal of Urology (1976), **48**, 127-134 ©

Male Epispadias: Surgical Repairs of Urethropenile Deformity

EMIL A. TANAGHO
Division of Urology, University of California School of Medicine, San Francisco, California

Unlike hypospadias, epispadias is relatively rare and is mostly seen in conjunction with bladder exstrophy. Complete simple epispadias presents an infrequent but challenging problem, not only because of the complete urinary incontinence commonly associated with it but also for the penile deformity and the urethral deficiency it displays. Hypospadias also manifests combined penile and urethral deformity but one can venture to say that its surgical correction has reached the point of perfection. We are a long way from this excellence in the repair of epispadias.

In 1869 Thiersch advocated the use of neighbouring skin flaps. In 1895 Cantwell, later followed by Bullitt (1903), developed his now classic rationale for urethral reconstruction—done by enfolding the urethra between the separate corpora. His emphasis was on urethral reconstruction rather than on correction of the penile deformity. Young, in 1918, revived interest in repair of epispadias and, in 1922, reported excellent results in the correction of urinary incontinence.

Ladd and Larman, in 1940, chose for repair of exstrophy with epispadias a technique using a flap from the mobilised bladder base to form the roof of the urethra. In 1952 Gross and Cresson published very good results, particularly regarding incontinence and urethral construction. Hinman, in 1958, was the first to emphasise the importance of lengthening the penis in the repair of exstrophy—a principle that can be applied for simple epispadias.

Welch, in 1962, revived Cantwell's technique and advocated separation of the unconnected pubic bones to permit the important step of mobilisation and repair of the bladder neck. He was less concerned about the correction of penile deformity.

Burkholder and Williams (1965) reported on their successful control of urinary incontinence for which they used a modification of the Young-Dees operation. Penile lengthening was accomplished in 4 of their 17 patients.

We have been unenchanted by our results with these techniques, particularly in relation to functional and cosmetic penile repair. In consequence, we have developed a different approach to the surgical repair of simple complete epispadias, with variations for incomplete epispadias. Epispadias as a part of bladder exstrophy presents a totally different surgical problem: it will not be discussed in this presentation.

Anatomic Deformity in Epispadias

By careful examination of a sagittal section of a complete epispadias, and comparison to the normal, the anatomical aberration can be clearly defined (Fig. 1). From this definition a rationale of repair can be formed. In complete epispadias the pelvic bones are most often separated to a variable degree and joined by a fibrous band. The short incompletely developed proximal urethra, instead of pointing downward toward the perineum, is pointing upward and is located anteriorly just below the flat pubic fibrous band to which it firmly adheres. It is also adherent to the rudimentary proximal portion of the corpus spongiosum and thus pulls it forward, making the penile base cling to the pubic band. The urethra is usually very short: by spreading the meatus one can see the verumontanum and look inside the dark bladder cavity.

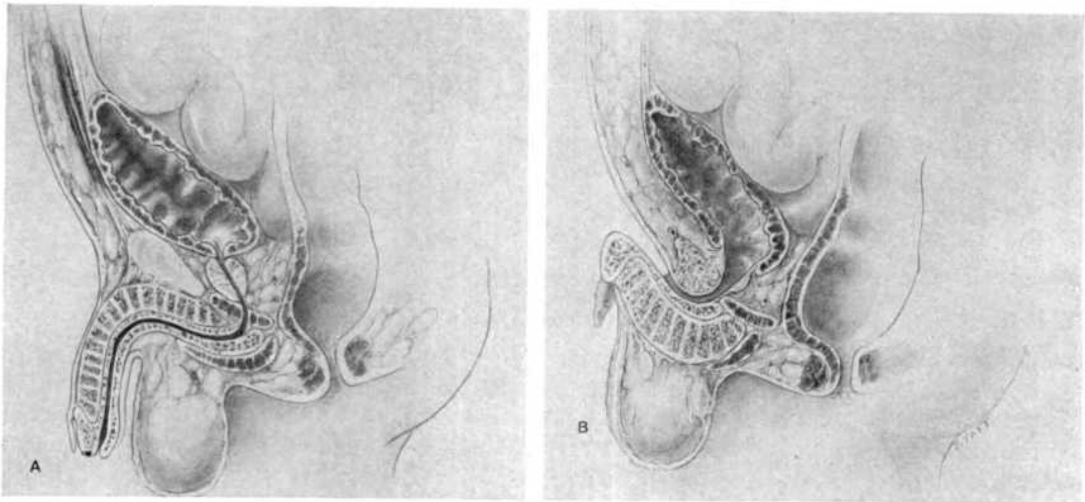


Fig. 1. (a) Sagittal section of normal male pelvis; (b) Anatomy of complete epispadias. Funnelled bladder neck. Short anteriorly displaced urethra adherent to pubic fibrous band, short curved penis and anteriorly overriding scrotum.

The bladder outlet is widely funnelled because of fibrous bands pulling on it all around its circumference. The prostate is generally rudimentary. It may even be indistinguishable as such, being incorporated into the funnelled part of the bladder outlet. The distal corpus spongiosum, being fibrotic, adds to the penile curvature and shortness.

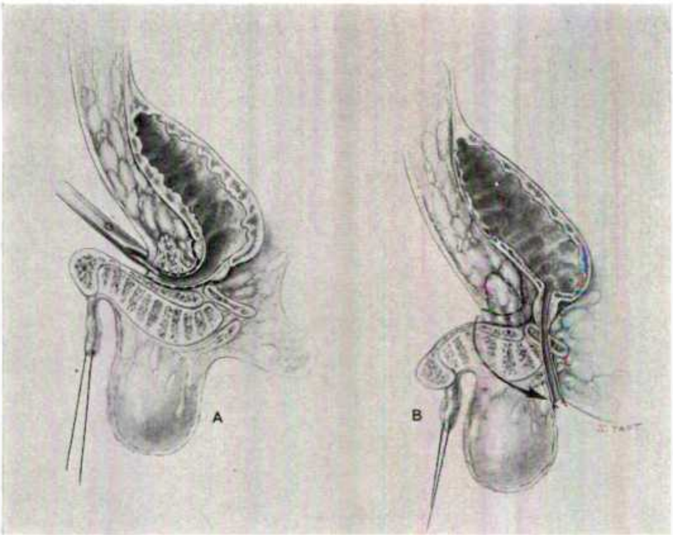
The scrotum is also noticeably displaced forward, overriding the ventrum of the penis and leaving behind it a wider perineum. The corpora cavernosa are usually widely separated as they diverge to gain attachment in the broadly separated pubic bonds. The epispadiac glans penis has a characteristic flattened splayed appearance with a ventral preputial hood.

Surgical Technique

The purpose of the surgical repair is to revert the abnormal anatomic features to the normal: the urethra should be freely mobilised and allowed its natural downward curve toward the perineum and continue on the floor of the penis. The bladder neck, the urethra, the corpora and the crura should all be freed from the pubic band to allow for satisfactory anatomic reconstruction permitting penile lengthening and mobility and for elimination of curvature of the penis as well as replacement of the urethra in the normal position.

Figure 2 illustrates its essential feature: complete mobilisation of the urethra from its firm fibrous adherence to the pubic band and all around its circumference. This dissection should not be stopped at the level of the apex of the prostate or verumontanum as suggested by Burkholder and Williams (1965) but should be continued all the way up to the level of the internal meatus and even beyond, for about 1 cm on the anterior and lateral bladder wall, as well as behind the trigone. The dissection should be done all round the circumference of the urethra and not limited to its anterior and posterior aspects. We have repeatedly noticed that, when these steps are completed, the funnelled bladder outlet assumes a more tubular form—as if it had been forced open in a funnel shape by the adhesions pulling on it all round its circumference. We have also noticed that, once the urethra and the bladder neck are freely mobilised, the urethra tends to tilt itself to point downward as it normally does.

The dissection is carried through the progressively widening space below the fibrous pubic band after circumscribing the epispadiac urethral opening and including with it the strip of urethral mucosa over the dorsum of the penis. The initial incision is seen in the dotted line in Figure 3. As dissection around the proximal urethra proceeds, one will notice the separation of the crura diverging toward the separated pubic arch. The corpus spongiosum will also be seen to be split apart at its origin. Dissection will be carried retropubically from the prepubic initial entry: this may seem difficult but, as this expanse becomes wider with progression of the procedure, it can easily be accomplished. Care should be taken to stay outside the prostatic capsule posteriorly in order not to injure it or its innervation. As mentioned before, the urethra, once fully mobilised, will tend to point downward. A blunt pathway could be readily developed between the diverging crura, then forcibly through the perineum, to come out the



UNIVERSITY COLLEGE OF MEDICINE
LIBRARY

Fig. 2. (a) Urethra and bladder neck are dissected (dotted line); (b) Urethra is then mobilised and brought down through genito-urinary diaphragm to peniscrotal junction as a perineal urethrotomy.

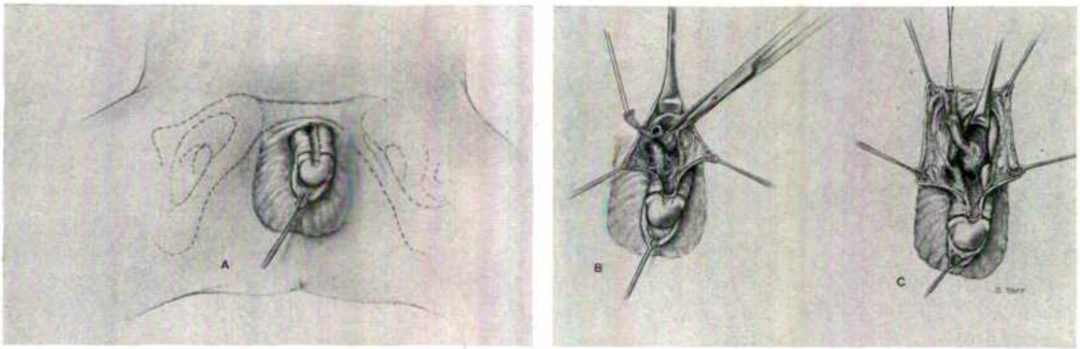


Fig. 3. (a) Initial incision (dotted line); (b) Urethra and cutaneous strip on dorsum of penis are being dissected and followed below pubic band; (c) Urethra and bladder neck completely mobilised; (d) Urethra completely mobilised. Crura are partially separated from the pubic arch. Note penile lengthening. Urethra is brought within bifurcated crura through genito-urinary diaphragm to perineum.

perineoscrotal junction where a stab wound is made and the urethra pulled through. A wide perineal urethrotomy is done, taking advantage of the mucosal strip attached to the urethra to obtain a wide suture line.

Attention is then diverted to free the crura from the fibrous pubic bands as well as from the pubic arch. Blood supply and innervation of the crura enter the distal third of its attachment to the pubic arch. Freeing the anterior third or one-half of this attachment will not interfere with innervation or blood supply. Once this is accomplished one will immediately notice marked lengthening of the penis, now free from the limiting fixed urethra on top of it and from its attachment to the pubic band. As a matter of fact the penis will be quite mobile and would drop all the way down if it were not for the overriding anteriorly displaced scrotum and the peniscrotal fold which tends to hold it up. Partial freeing of the crura from the pubic arch helps appreciably in gaining penile length.

The next step consists of complete denudation of the penis from its skin covering by continuing the incision all around the prepuce (Fig. 4). Occasionally there remain limiting fibrous bands in the dorsum, which can be either excised or incised transversely to achieve complete elimination of the curvature. If one now pulls on the peniscrotal fold, away from the penis, the latter will fall directly downward. By blunt dissection a scrotal space is developed and a transverse incision is made, slightly anterior to midscrotum; the mobilised penis is allowed to drop downward into the scrotal sac and its glans to protrude through the scrotal incision (Fig. 4c). The body of the penis is left imbedded in the scrotum. Similar steps have been described by Michalowski and Modelski in 1963.

Attention is then directed to the penile skin and the prepuce: the latter is unfolded and the former is stretched and turned into a tube while still attached to the abdominal wall at its base, at the initial root of the penis. Its free end is then anastomosed to the perineum, just distal to the newly developed perineal urethral opening (Fig. 5). Completion of the first stage of the repair is now done.

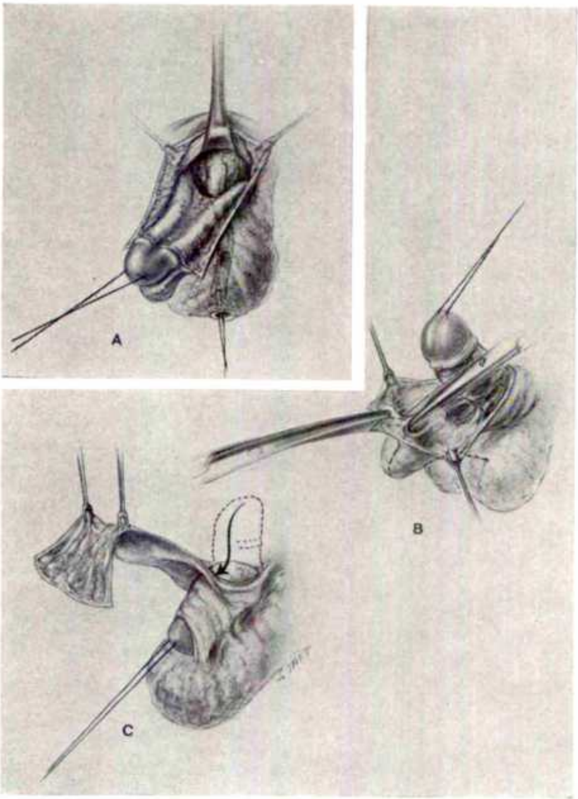


Fig. 4. (a) Penis is being denuded of its skin; (b) Prepuce is unfolded then split in midline; (c) A pouch is bluntly developed in which penis will lie and glans penis will protrude through a transverse incision in midscrotum.

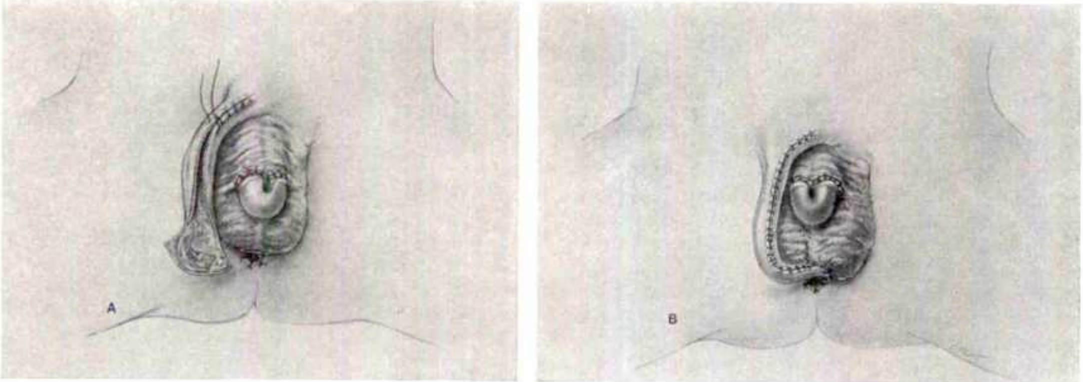


Fig. 5. (a) Unfolded preputial and penile skin is closed into a skin tube; (b) Closure of skin tube is completed. Tube is sutured to a transverse incision proximal to perineal urethrotomy.

The second stage is carried out 4 to 6 months later, after oedema and skin reaction have subsided. With the use of an NM type of incision the penis is freed from the scrotum (Fig. 6). The scrotal defect is then closed underneath. The perineal urethral opening and the penile skin tubes are still present.

The third stage is done again 4 months later when the penile skin tube is detached from its upper attachment and split open in the midline. Another midline incision is made on the ventrum of the penis and midscrotum all the way down to the pedicle of the tube. This incision has to be carried deep enough to expose Buck's fascia in the entire length of the incision (Fig. 7).

The split skin tube is then sutured to the edge of this midline peniscrotal incision. Midline subcutaneous suture

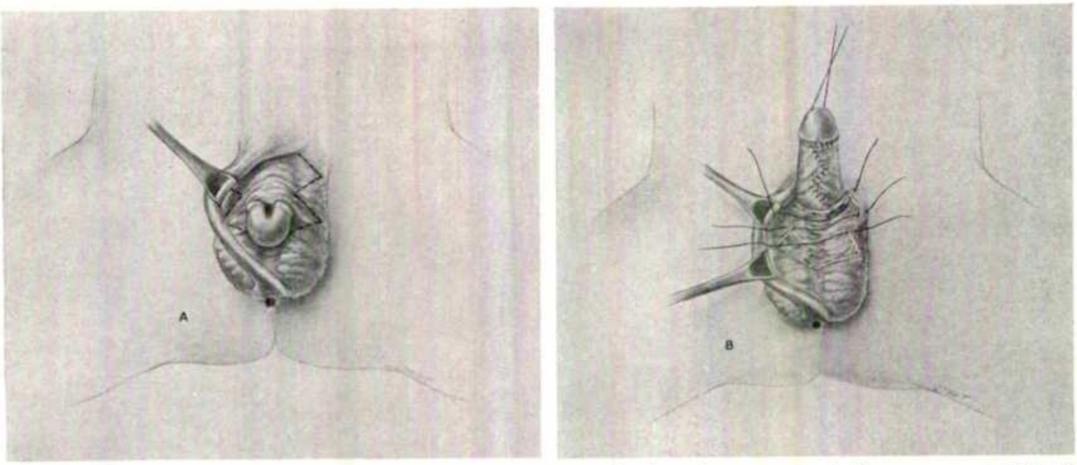


Fig. 6. Stage II. (a) Dotted line shows an NM incision in scrotum, allowing adequate scrotal skin to wrap around penis; (b) Penis is lifted from scrotum with adequate skin. Scrotal incision is being closed. Penile skin tube is intact.

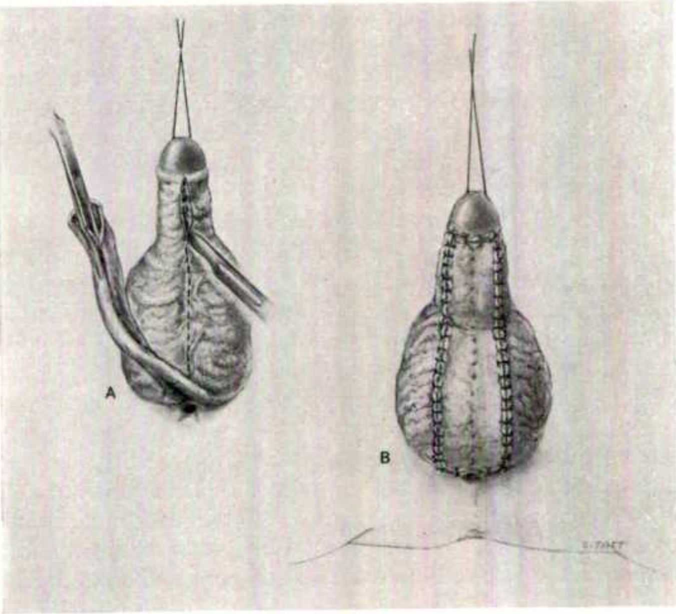


Fig. 7. (a) Midline incision is made in ventral surface of penis and in midscrotum carried deep to Buck's fascia. Penile tube is disconnected from its prepubic attachment and is split open on opposing midline; (b) Splayed skin flap is sutured in place, care being taken to suture it in midline to Buck's fascia so that it will stick deep in midscrotum.

should fix the centre of the skin flap deep to Buck's fascia. This penile skin implant is the best for urethral reconstruction and should be fixed deep into the cleft in the midscrotum to develop firm adherence to the penile body. The result is a bifid scrotum with a strip of soft stretchable penile skin in between. In the fourth stage of the procedure this penile skin strip is turned into a urethral tube (Fig. 8). It is now in a deep normal position.

At the same time, or preferably at another stage, the splayed dorsal aspect of the glans penis is denuded of its skin and its halves closed by several layers closure. This final step completes the penile and urethral reconstruction.

Discussion

Urinary incontinence is commonly associated with epispadias but is deliberately not discussed in this presentation since it is a separate entity requiring its own specific management. Regardless of incontinence, of its correction, or of the institution of urinary diversion, an operation for repair of penile deformity and urethral deficiency is mandatory.

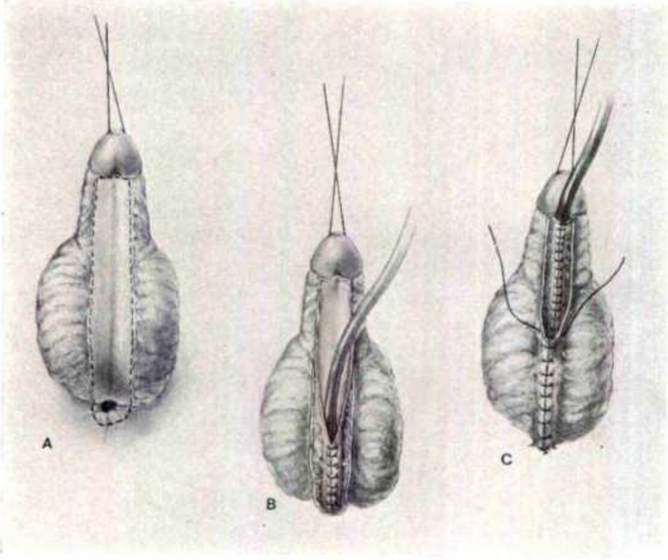


Fig. 8. Final stage, when completed penile skin strip will be turned into a tube for urethral reconstruction. (a) Dotted line of incision; (b) Formation of urethral tube; (c) Covering of urethra by mobilised adjacent skin.

Several techniques have been described. Urethral reconstruction by one method or another has been invariably successful, whether accomplished in 1 or several stages. Correction of penile deformity has been less satisfactory. Advocates and adversaries of iliac osteotomy have debated its efficiency in approximating the widely separated pubic bone and thus improving penile deformity. Some (Caskie and Borsky, 1958; Shultz, 1958; Guthrie, 1974) claim that it is extremely helpful in lengthening and straightening the penis, while others (Williams and Savage, 1966; Marshall and Muecke, 1970; Johnston and Kogen, 1974) believe that the associated inward pubic bone rotation further accentuates the deformity. Relocation of the widely separated crura on the pubic arch by chiselling them off from the pubic bone and advancing them more forward is theoretically sound. However, this radical approach involves the danger of denervation and devascularisation, with impotence as a result.

The partial freeing of the crura from the pubic bone accomplishes adequate freeing and lengthening, yet does not endanger nerve and blood supply.

We feel that the principle of completely freeing the body of the penis from the urethra, bladder neck and fibrous pubic band is basic for penile lengthening and straightening. Once this is done, not only will the urethra and bladder outlet assume a more normal position and inclination but the penis itself will be able to drop downward. The only limiting factors to perfect reconstruction are the degree of separation of the pubic rami and the initial size of the penis. The anteriorly displaced scrotum and the peniscrotal fold are also agents holding the penis upward. This difficulty is easily circumscribed by dropping the penis into the scrotum and relocating it later in a more normal downward position.

Little can be done to the initially rudimentary or small penis. Hormonal therapy might be beneficial but our experience has not included this approach. For widely separated pubic rami, osteotomy may be considered.

During the last 6 years we have encountered 12 cases of epispadias: 4 were female, with incontinence—in whom bladder neck reconstruction was done; 3 are currently continent and the 4th markedly improved; no urethral reconstruction was done. 8 were male, 3 of whom were seen before any surgical intervention had been attempted and the remaining 5 after unsatisfactory partial or complete reconstruction had been done. Our technique was applied either *in toto* or partially modified, according to the case. Results have generally been very gratifying. We dare say that, before our adoption of this method, we had never seen completely satisfactory penile correction in any case of complete epispadias. We and others using the same procedure have repeatedly witnessed marked improvement of the defect. In the 5 cases of penile reconstruction considered adequate by some, but judged unsatisfactory by us, great improvement was achieved when our principles of repair were applied. Minor modification of the technique can be used for incomplete epispadias, according to the severity of the curvature and the urethral deficiency.

We do not claim this technique to be original. Most of the steps of the repair have been utilised in one or other type of plastic repair. The original step of the procedure, however, is that of complete mobilisation of the urethra and the bladder neck region and relocation of the urethra in a more normal position. When it is coupled with complete freeing of the crura, satisfactory reconstruction of both penile deformity and urethral deficiency can be accomplished.

Summary

A surgical technique for the repair of complete epispadias, with emphasis on correction of the urethropenile deformity and attempt to restore normal anatomic relations has been presented.

The epispadiac orifice is dissected and followed proximally to beyond the bladder neck, then brought out perineally between the bifurcated crura. The penis is denuded from its skin, then embedded in the scrotum, except for the glans penis which protrudes from the midscrotum.

Penile skin is folded into a tube to be used later for urethral reconstruction.

Excellent cosmetic and functional results are consistently obtained by this multi-stage technique.

References

Bullitt, J. B. (1903). Epispadias. Report of a case operated on by a modification of Cantwell's method. *Journal of the American Medical Association*, **41**, 297-300.

Burkholder, G. V. and Williams, D. I. (1965). Epispadias and incontinence: surgical treatment of 27 children. *Journal of Urology*, **94**, 674-679.

Cantwell, F. V. (1895). Operative treatment of epispadias by transplantation of the urethra. *Annals of Surgery*, **22**, 689-694.

Caskie, J. D. and Borski, A. A. (1963). One-stage plastic repair of exstrophy of bladder combined with bilateral osteotomy of the ilia. *Journal of Bone and Joint Surgery (American)*, **45-A**, 161-164.

Dees, J. E. (1942). Epispadias with incontinence in the male. *Surgery*, **12**, 621-630.

Dees, J. E. (1949). Congenital epispadias with incontinence. *Journal of Urology*, **62**, 513-522.

Gross, R. E. and Cresson, S. L. (1952). Treatment of epispadias: a report of 18 cases. *Journal of Urology*, **68**, 477-488.

Guthrie, T. Personal communication.

Hinman, F. (1957, 1958). A method of lengthening and repairing the penis in exstrophy of the bladder. *Transactions of the American Association of Genito-Urinary Surgeons*, **49**, 23-27. *Journal of Urology*, **79**, 237-241.

Johnston, H. and Kogen, S. (1974). The exstrophic anomalies and their surgical reconstruction. In *Current Problems in Surgery*. Chicago: Yearbook Medical Publishers, pp. 4-39.

Ladd, W. E. and Larman, T. H. (1940). Exstrophy of the bladder and epispadias. *New England Journal of Medicine*, **222**, 130-134.

Marshall, V. F. and Muecke, E. C. (1970). Functional closure of typical exstrophy of the bladder. *Journal of Urology*, **104**, 205-212.

Michalowski, E. and Modelski, W. (1963). The surgical treatment of epispadias. *Surgery, Gynècology and Obstetrics*, **117**, 465-468.

Shultz, W. G. (1958). Plastic repair of exstrophy of bladder combined with bilateral osteotomy of ilia. *Journal of Urology*, **79**, 453-458.

Thiersch, C. (1869). Ueber die Entstehungsweise und operative Behandlung der Epispadie. *Archives der Heilkunde*, **10**, 20-35.

WELCH, K. J. (1962). Epispadias. In *Pediatric Surgery*, ed. by C. D. Benson *et al.* Chicago: Yearbook Medical Publishers, pp. 1082-1089.

WILLIAMS, D. I. and SAVAGE, J. (1966). Reconstruction of the exstrophied bladder. *British Journal of Surgery*, **53**, 168-173.

YOUNG, H. H. (1918). A new operation for epispadias. *Journal of Urology*, **2**, 237-251.

YOUNG, H. H. (1922). An operation for the cure of incontinence associated with epispadias. *Journal of Urology*, **7**, 1-32.

The Author

Emil A. Tanagho, MD, Professor of Urology.

Requests for reprints to: Dr E. A. Tanagho, Division of Urology A-644, University of California, San Francisco, California 94143.

British Journal of Urology (1976), **48**, 135-138 ©

An Unusual Case of Right and Left Testicular Arteries Arching over the Left Renal Vein

HILEL NATHAN, PHILIP V. TOBIAS and MICHAEL D. WELLSTED

Department of Anatomy and Anthropology, Sackler Medical School, Tel Aviv University, Israel and Department of Anatomy, University of the Witwatersrand Medical School, Johannesburg, South Africa

Variations in the anatomical relationship of the gonadal arteries to the renal vessels are both frequent and multiform (Gerard, 1913; Spivack, 1933; Cordier *et al.*, 1938; Pick and Anson, 1940; Sauramo, 1945; Notkovich, 1955, 1956; Merklin and Michaels, 1958). Most of these variations were described and classified by one of the present authors (Notkovich, 1956), who in the same paper suggested the developmental mechanisms possibly underlying these anomalies. One of the variations, a left gonadal artery arching over the left renal vein, was of particular significance since it was considered to be an important factor in the aetiology of varicocoele and/or orthostatic proteinuria on the same side (Notkovich, 1955; Nathan, 1958; Nathan and Orda, 1968).

The present paper describes a case in which both right and left testicular arteries arched over the left renal vein. Such a variation has not previously been encountered in more than 1500 dissections of the renal pedicle, nor has it been described in the anatomical literature to the best of our knowledge.

Material and Description

The cadaver of an adult South African Negro male (Number AD 4451), dissected in the Anatomy Department of the University of the Witwatersrand, Johannesburg, presented the following features (Fig. 1).

The kidneys and renal vessels were normal in size, position, number and relations except with regard to the right and left testicular arteries. The latter arteries took origin from the anterior aspect of the abdominal aorta below the renal vessels, ascended behind the left renal vein and arched over its superior aspect. They then descended in front of the left renal vein to meet and accompany the corresponding testicular veins and follow their normal course to the inguinal canals.

The arch of the left testicular artery was lateral to (or to the left of) the entrance of the left suprarenal vein into the renal vein, while that of the right testicular artery was medial to (or to the right of) the left suprarenal vein. The right testicular artery then proceeded downwards and to the right, crossing anterior to the stem of the left renal vein and then in front of the inferior vena cava to reach the corresponding testicular vein (Fig. 1).

Distinct impressions were observed on the left renal vein, produced by the arches of the testicular arteries.

Discussion

This arching configuration of the gonadal arteries conforms broadly to the Type III pattern of variation previously described by Notkovich (1956). However, in all the Type III cases then described, each gonadal artery arched over the renal vein belonging to the same side of the body as the artery. Thus, in a series of 405 dissections of gonadal vessels in 183 cadavers (some of which had multiple gonadal vessels) the left gonadal arteries arched over the left renal vein in 20·7% and the right gonadal arteries arched over the right renal vein in 7·6%.

The course of the testicular arteries described here is unique, in that not only the left testicular artery but also the *right artery arched over the left renal vein*, a relationship not previously described or observed.

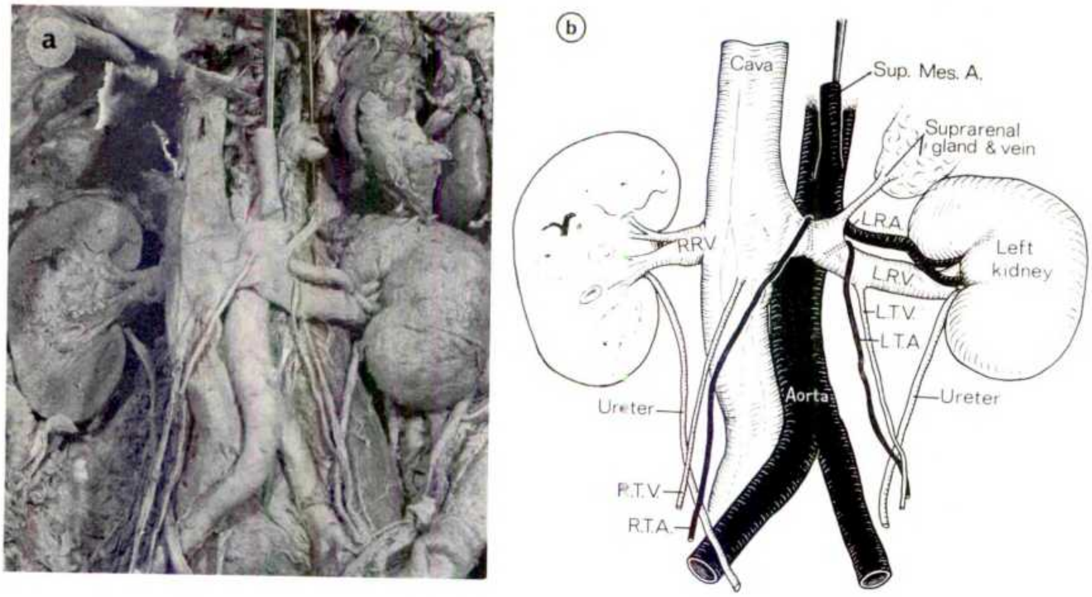


Fig. 1. (a) and (b) to show the left and right testicular arteries arching over the left renal vein on either side of the entry of the left suprarenal vein. The actual origin of the testicular arteries from the abdominal aorta is not seen, as the arteries arise under cover of the left renal vein.

Key: L.R.V., Left renal vein. L.R.A., Left renal artery. L.T.A., Left testicular artery. L.T.V., Left testicular vein. R.T.A., Right testicular artery. R.T.V., Right testicular vein. R.R.V., Right renal vein. Sup. Mes. A., Superior mesenteric artery.

A full description has earlier been given of the possible developmental mechanisms leading to the variations of the gonadal arteries (Notkovich, 1956). The mechanism proposed then to explain the arching of the gonadal artery over the ipsilateral gonadal vein was that 1 or more of the gonadal arteries originating cranial to the renal vein persisted and, further, that the kidney ascended to a higher level than the origin of the gonadal artery. This twofold set of circumstances forced the gonadal artery to follow an arched course over the corresponding renal vein, thus producing the Type III variant. It is suggested that the same explanation may be applied to the right testicular artery arching over the left renal vein, which in fact is the unusual observation of the present paper. Again, the persistence of gonadal arteries originating cranial to the renal veins and their deflection by those veins following ascent of the kidney explain the facts observed in this case (Fig. 2).

Besides the developmental and morphological interest of such cases they have practical importance from the clinical or pathological viewpoint. Compression of the left renal vein by the arteries, particularly when the subject is in the erect position, may raise the venous pressure in the vein and be a factor in the aetiology of varicocoele and proteinuria (Notkovich, 1955, 1956; Nathan, 1958, 1963; Bailey and Love, 1962; Nathan and Orda, 1968; Iuchtman, 1975). The outcome of renal vein compression may depend on the presence or absence of venous anastomotic channels between the renal veins and the vertebral, hemiazygos or other parietal venous systems draining into the caval veins. Such anastomotic channels have been described in varying frequencies (Lejars, 1888; Faragasanu, 1938; Anson and Cauldwell, 1947; Notkovich, 1956).

Finally, awareness of the possible existence of such variations in the course of the gonadal arteries, in relation to the renal veins, is of importance during surgery in this region.

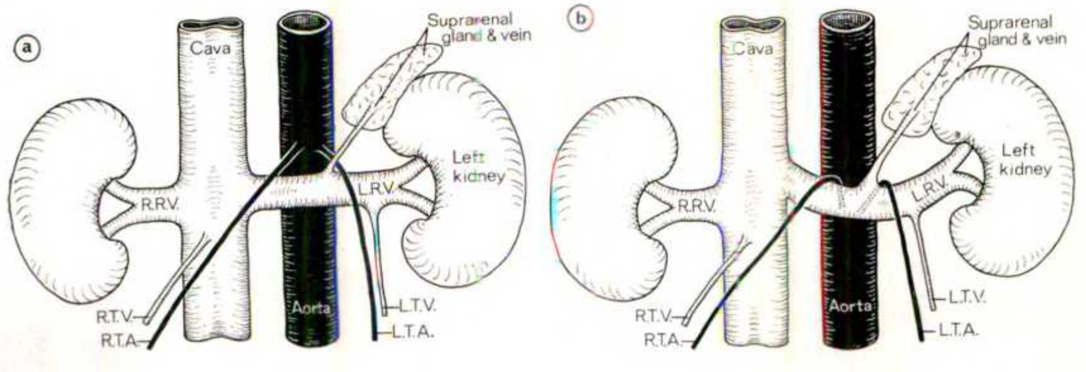


Fig. 2. 2 stages in the formation of the newly described variant. (a) Persistence of the testicular arteries cranial to the renal veins; (b) Ascent to the (left) kidney with consequent deflection and arching of the testicular arteries over the left renal vein.

Summary

An unusual case in which both testicular arteries arched over the left renal vein is described.

A developmental explanation for the unusual vascular pattern is given.

The possible importance of this and similar anomalies in the causation of varicocoele and orthostatic proteinuria is discussed.

The authors are grateful to Mr P. Faugust of the Witwatersrand University Department of Anatomy for the photography and to Mrs K. Copley and Miss N. Gruskin for preparation of the manuscript.

References

Anson, B. J. and Cauldwell, E. W. (1947). The pararenal vascular system. *Quarterly Bulletin of Northwestern University Medical School*, **21**, 320-328.

Bailey, H. and Love, M. (1962). *A Short Practice of Surgery*, 12th ed. London: Lewis, p. 1275.

Cordier, P., Devos, L. Delcroix, A. and Renier, M. (1938). Variations du traject de l'artère spermatique. *Annales d'anatomie pathologique et d'anatomie normale medico-chirurgicale*, **15**, 535-536.

Faragasanu, I. (1938). Recherches anatomiques sur la veine rénale gauche et ses collatérales. Leurs rapports avec la pathogénie du varicocèle essentiel et des varices du ligament large. *Annales d'anatomie pathologique et d'anatomie normale medico-chirurgicale*, **15**, 9-52.

Gerard, G. (1913). Sur les variations d'origine et de nombre des artères génitales, spermatiques ou ovariennes de l'homme. *Comptes Rendus de la Societé de Biologie*, **74**, 778.

Iuchtman, M. (1975). Caval and renal vein compression of arterial origin. *International Surgery*, **59**, 524-526.

Lejars, F. (1888). Les voies de sûreté de la veine rénale. *Bulletin de la Société Anatomique de Paris*, **63**, 504-511.

Merklin, R. P. and Michaels, N. A. (1958). The variant renal and suprarenal blood supply with data on the inferior phrenic, ureteral and gonadal arteries. *Journal of the International College of Surgeons*, **29**, 41-46.

Nathan, H. (1958). Observations on aberrant renal arteries curving around and compressing the renal vein. *Circulation*, **18**, 1131-1134.

Nathan, H. (1963). Aberrant renal artery producing developmental anomaly of kidney associated with unusual course of gonadal (ovarian) vessels. *Journal of Urology*, **89**, 570-572.

Nathan, H. and Orda, R. (1968). Etiologia de varicocele esencial. *La Prensa Médica Argentina*, **55**, 1498-1502.

Notkovich, H. (1955). Testicular artery arching over renal vein: clinical and pathological considerations with special reference to varicocele. *British Journal of Urology*, **27**, 267-271.

Notkovich, H. (1956). Variations of the testicular and ovarian arteries in relation to the renal pedicle. *Surgery Gynecology and Obstetrics*, **103**, 487-495.

PICK, J. W. and ANSON, B. J. (1940). The renal vascular pedicle. *Journal of Urology*, **44**, 411-434.

SAURAMO, H. (1945). Ueber die Uteroovarialen Blutgefässe. *Annales Academiae Scientiarum Fennicae*, series A.V., Medica-Anthropologica, 3.

SPIVACK, J. A. (1933). Unusual course of the internal spermatic artery. *Urologic and Cutaneous Review*, **37**, 322-324.

The Authors

H. Nathan, MD, Chairman, Department of Anatomy and Anthropology, Sackler Medical School, Tel Aviv University. Former name H. Notkovich, now H. Nathan.

P. V. Tobias, DSc (Witwatersrand), FRSSAf, FLS, Head, Department of Anatomy, University of the Witwatersrand.

M. D. Wellsted, MB, BCh, Lecturer, Department of Anatomy, University of the Witwatersrand.

British Journal of Urology (1976), **48**, 139-144 ©

A.I.D.—A Review of 200 Cases

ROBERT NEWILL
Endocrine Unit, Department of Obstetrics and Gynaecology, University College Hospital, London

Very little has been written in British medical journals about the problems associated with artificial insemination from a donor (A.I.D.). This is probably because A.I.D. is a medical service which in the United Kingdom is almost confined to private medicine and is done only rarely in National Health Service hospital practice.

This is a review of 200 childless couples referred for A.I.D. in the past 2 years by gynaecologists, urologists and general practitioners.

The Patients

The reasons for referral are shown in Table I. By far the most common cause of requests for A.I.D. were azoospermia or oligospermia in the husband and presumed normal fertility in their wives. Almost all the husbands referred by urologists or seminologists had had adequate investigations and treatment. The commonest identified causes of subfertility in these men were varicocele, undescended testes which had been brought down into the scrotum after infancy and maturation arrest of unknown cause during spermatogenesis.

With one exception, these young couples all had stable marriages which had survived the emotional trauma of years of failure to conceive and of infertility investigations, culminating in the knowledge that the husbands were incapable of impregnating their wives; one couple asked to stop A.I.D. because of impending divorce.

Up to a few years ago couples in this position would have been advised to adopt children and it is generally believed that most would still do so if babies for adoption were freely available. However, in talking to these couples, it is apparent that the majority who have made the decision for donor insemination would still do so even if there were no shortage of babies for adoption.

The probable reason for this is that women who feel themselves capable of bearing children prefer to mother their own natural children and their husbands understand this and feel that it is preferable for the children in their home to be brought up by at least one natural parent. Also these couples intend to bring up their children as normal legitimate children thus avoiding, as they hope, all the emotional and administrative problems of adoption. A.I.D. also enables a couple to have a child fathered by a man from the same social background as themselves.

To all their friends and relations the infertile husbands appear to have fathered these children which helps these men to adopt the role of putative fathers to their wives' children. When women return for a second child by A.I.D., they are asked if their husbands have accepted the first child as their own and in every case so far the answer has been in the affirmative. Presumably the husbands would not have consented to A.I.D. if there had been any doubts in their minds whether they would accept the children.

To many people the deception of the children inherent in A.I.D. is improper but the couples themselves who have requested donor insemination feel that this is an acceptable way of bringing children into their homes. It remains their responsibility to decide whether to tell their children how they are conceived. In those cases where A.I.D. is done because the husband's family carries an unpleasant unifactorial hereditary disease (tuberose sclerosis, Huntington's chorea, etc.) I advise people to tell their children when they have reached a mature age; otherwise the children will worry unnecessarily that they may be carrying the unpleasant gene.

Table I

Reasons for Referral for A.I.D.—Male Factors

Reason	Number	Comments
Rhesus incompatibility	2	For rhesus negative donors
Unifactorial genetic disease in husband's family	2	Tuberose sclerosis and Huntington's chorea
Azoospermia	93	
Oligospermia	85	
Necrospermia	1	
Hostile mucus of sperm antibodies	3	Two became pregnant by their own husbands
Retrograde ejaculation	2	
Impotence and unable to produce masturbation specimens for A.I.H.	4	
Paraplegia	2	Unable to produce specimens for A.I.H.
Iatrogenic azoospermia	2	Treated for Hodgkin's disease
Bilateral orchidectomy for testicular tumours	1	
Klinefelter's syndrome	3	All had azoospermia
Total	200	

The Donors

In this series the donors were nearly all medical students from London teaching hospitals. The medical profession is still held in high enough respect for potential doctors to be acceptable to all these couples as the fathers of their children. A few non-European donors were recruited from other sources, *e.g.* the London School of Economics and the School of African and Oriental Studies, as there are no longer any African or Arab undergraduates at the London teaching hospitals. Recruitment of donors from ethnic groups other than European is exceptionally difficult owing to the reluctance of young men from these groups to offer themselves as donors.

Donors were interviewed to ascertain their physical characteristics, social backgrounds and special talents so that they could be matched as nearly as possible to the recipient couples. Donors were blood grouped and some were screened for venereal disease. There is no point in being too obsessional about screening for V.D. since this is uncommon in medical students and there is no guarantee that a young man who is free from infection at the first screening will not contract the disease later. Examination of all donated semen specimens under the microscope has not revealed any evidence of infection in any of them. Neither were they screened for genetic disease, because rare, unpleasant hereditary diseases are unlikely to be discovered by karyotyping apparently healthy young men whose family medical history was assessed before they were accepted for medical school.

Since no child is an exact Identikit portrait of his parents, it is unnecessary to attempt to match the donor exactly to the husband. In this series, the blood group, eye colour and general racial characteristics (including northern or southern European characteristics) were matched but hair colour, which is not strongly hereditary, was not matched exactly. The babies born so far have all been accepted by their parents as being well-matched to themselves. Jewish patiënts almost always requested a Jewish donor and this was arranged.

The motive of these young men in offering themselves as donors of semen was almost certainly the fee paid for each specimen (£4), though a secondary motive was to assure themselves of their own fertility. Only one student offering himself as a donor was found to be azoospermic; the others had variable fertility. Some donors were always highly fertile while the fertility of others varied considerably and it was noticeable that the fertility of these latter students could be affected considerably by illness or the stress of examinations.

Table II

Results of Pregnancies

Healthy babies born, male	23 (two pairs male twins)
Healthy babies born, female	32 (one pair female twins)
Defective babies (one m. one f.)	2
Neonatal death, male	1
Miscarriages	8 (one of twins)
Pregnancies in progress	44
Total	110

Experience of looking at large numbers of semen specimens makes it possible to recognise certain characteristics, crystals, leucocytes, etc., which are always present in the semen of certain donors so that it is frequently possible to identify a donor by microscopic examination of his semen.

The maximum number of pregnancies produced by any one donor was 4 spread over a wide area of the country, so the chance of half-siblings meeting and marrying in the future is very remote.

Technique

Fresh semen was used entirely. Although the use of fresh semen requires considerably more organisation than the use of frozen semen, the pregnancy rate is higher. The semen specimens were delivered about an hour before the recipients arrived and were placed in an incubator. The donors and recipients, of course, never met each other. If the motility of the sperms was poor on delivery, 5·5 mmol of caffeine citrate (1 ml of a 10% solution) was added to the total specimen (Haesungcharern and Chulavatnatol, 1973; Schoenfeld, Amelar and Dubin, 1973).

1 ml of fresh semen was introduced through an insemination cannula into the cervical canal and the patient remained lying on her back for 5-10 min by which time most of the more active sperms were well established in the cervical mucus.

The actual technique of A.I.D. is therefore simple but the administrative problems, when using fresh semen, of getting the donor and recipient together on the correct day are considerable. These administrative problems can be lessened by the use of frozen semen from a bank and although American workers (Steinberger and Smith 1973) have achieved good results with frozen semen it is not nearly so effective as fresh semen unless the semen to be frozen is selected with great care. The use of a frozen semen bank also greatly increases the cost of A.I.D.

Results

At the time of writing 110 of these 200 women have become pregnant, 27 have abandoned A.I.D. for various reasons, 5 have become pregnant by their husbands and the remaining 58 are still attending for A.I.D. Only 18 of the current 58 have been trying for over a year. About 85% of women will achieve pregnancy by A.I.D. if they persevere.

Of the 58 babies so far born to these women there have been 2 sets of binovular twins, 1 anencephalic fetus, 1 neonatal death from pulmonary atelectasis and 1 premature baby with a neural tube defect who died soon after birth. The twins were healthy and all the remaining babies were normal, healthy infants. The anencephalic fetus is not considered to be the result of any paternal factor since the donor concerned had already fathered one healthy baby. During investigation of the congenitally defective infant, the mother admitted having had intercourse with her neighbour the day after the insemination so there is some doubt about the actual father of this child.

32 of the babies already born are girls and 23 are boys. This considerable preponderance of girls is in contrast to most previously published figures for donor insemination (Seymour and

Table III

Infertility Factors in Wives

Secondary amenorrhoea	1	
Galactorrhoea-amenorrhoea	1	(now pregnant after treatment with bromocriptine)
Oligomenorrhoea	6	
Anovular cycles	14	
Ovarian deficiency	61	(probable non-ovulation)
Endometriosis	3	
Tubal blockage or adhesions	2	
Total	88	

Koerner, 1941; Portnoy, 1956; Steinberger and Smith, 1973) in which male babies predominated. Langer, Lemberg and Sharf (1969) found no significant sex difference.

The reason for the female preponderance in this series is not obvious but on referring to these patients' records it appeared in general (and when only one insemination per month was done) that if the insemination was done before the apparent day of ovulation, from the basal temperature record, the baby was more frequently female whereas an insemination immediately after the rise in temperature was more likely to produce a male baby. Since most inseminations were timed just before the expected day of ovulation the resulting fetuses were more commonly female. However, this sex difference is in contrast to that of Marshall (1968) who, in a study attempting to show whether the age of spermatozoa affected congenital abnormality, found a sex ratio of 43 males to 28 females in the children born to women in whom coitus only took place before the rise in basal body temperature.

Infertility Factors in the Wives

Most women who present themselves for A.I.D. on the grounds of their husbands' infertility naturally assume that this is the reason for their failure to conceive. They believe that insemination with fertile semen will result almost immediately in pregnancy. However, this is very far from the case and many women only achieve pregnancy after several months of inseminations and after treatment of their own infertility factors. Probably one of the most potent factors in reducing a woman's fertility is years of trying to prevent pregnancy by the use of contraceptives or years of marriage to an infertile husband who cannot impregnate her. All couples are therefore warned not to expect a quick pregnancy unless the wife is exceptionally fertile.

During the first 2 or 3 months of A.I.D. many women, whose cycles have previously been regular, develop very irregular cycles varying between 24 and 35 days. This is undoubtedly an emotional effect since the "menstrual clock" of the hypothalamus is very sensitive to emotion and the stress of trying to get pregnant by unnatural means results in this disturbance of rhythm. Stress is a very potent factor in delaying ovulation or suppressing ovulation altogether and the effects of stress on ovulation have been investigated and described by several authors (Fremont-Smith and Meigs, 1948; Sturgis, 1962; Peyser *et al.*, 1973). Cycles varying by 10 days or more make the timing of insemination very unreliable so these women were given small doses of clomiphene (50 mgm daily for 3 or 5 days from day 3 of their cycles) and this usually made them revert to a 28-29 day cycle.

Most women had not had a full investigation of their own fertility since their husbands' infertility had usually been discovered at an early stage of the investigation. Almost all, however, had kept basal temperature records and many had also had endometrial biopsy or curettage. One notable feature was the number of women who produced past temperature records which were either quite meaningless or were doubtfully biphasic but which, nevertheless, had resulted in their being confidently assured that they were ovulating. Many women have no idea how to take their temperature accurately and there seems to be no definite criteria for the interpretation of a basal temperature chart and this tends to result in women being assured by inexperienced doctors that their temperature charts are quite normal when, in fact, they are not open to any accurate interpretation.

A.I.D. offers a good opportunity to study infertility in women because one factor in human fertility, the semen, is known and is constant. If highly fertile semen is placed into the cervical canal around the expected time of ovulation, and the woman persistently fails to become pregnant, it is reasonable to assume that some infertility factor exists in her. This happened very frequently in this series of cases and 82 women required some investigation of their own fertility. 75 women had anovular cycles or suspected non-ovulation which was judged from the basal temperature record, the mid-cycle absence of mucus, from endocrine cytology and from their failure to conceive. Most of this group subsequently became pregnant when they were started on clomiphene, suggesting that hypothalamic suppression due to stress was the cause of their ovarian deficiency.

One of the most interesting facts to emerge from this series is the number of women with borderline oligospermic husbands who were considered to be normally fertile and whose failure to conceive had been probably incorrectly attributed to their husbands' subfertility. 3 of these women did actually become pregnant by normal intercourse with their husbands when they were given clomiphene to stimulate ovulation, or to regulate their cycles, before A.I.D. was commenced. Several others, who only became pregnant after treatment with clomiphene, had borderline oligospermic husbands who might well be the fathers of their children and not the donors.

This state of affairs is the unfortunate result of the very unsatisfactory criteria at present used to diagnose ovulation in women. The usual tests employed by gynaecologists, *i.e.* the biphasic basal temperature record and a secretory endometrium in the second half of the menstrual cycle, have never been more than presumptive evidence of ovulation but long usage and the absence of any reliable test of ovulation have resulted in these tests being regarded as positive evidence of ovulation. Recent work on these tests however (Pennington, Beazley and Wilson, 1970; Cooke, Morgan and Parry, 1972), are tending to produce evidence that a secretory endometrium or a biphasic temperature record do not correlate with ovarian function and ought not to be used to assert dogmatically that any woman is ovulating.

This series of 200 cases suggests that in many couples both partners have some infertility factors and that oligospermic men, particularly if sperm motility is good, can impregnate their wives if the infertility factors in the latter are recognised and treated.

This difficulty in assessing ovarian function accurately is also liable to lead to the incorrect diagnosis of "hostile mucus" or "sperm antibodies" in some infertile women. 3 couples in this series were referred for A.I.D. because repeated post-coital tests had shown only dead sperms in spite of the husbands' excellent semen analyses. It was assumed that the wives had hostile mucus or had developed sperm antibodies and could never be impregnated by their husbands. Endocrine assessment of all 3 wives showed deficient follicular phases and, when this was corrected, all 3 had excellent sperm invasion tests with their husbands' semen. 2 have become pregnant by normal intercourse with their husbands and have delivered healthy babies.

Conclusion

A.I.D. is a useful and increasingly acceptable technique for bringing children into those childless homes in which the wives are capable of being mothers but their husbands are incapable of impregnating them.

Summary

200 consecutive cases of couples referred for A.I.D. are reviewed. The reasons for referral are given and the technique and donors are discussed. It is estimated that about 85% of women who receive donor insemination will achieve pregnancy if they persevere.

Infertility factors are common in women who present for donor insemination and this usually takes the form of ovarian follicular deficiency, probably with non-ovulation. It is suggested that a

biphasic basal temperature record or a secretory endometrium in the luteal phase are unreliable tests for ovulation.

References

COOKE, I. D., MORGAN, C. A. and PARRY, T. E. (1972). Correlation of endometrial biopsy and plasma progesterone levels in infertile women. *Journal of Obstetrics and Gynaecology of the British Commonwealth*, **79**, 647-650.

FREMONT-SMITH, M. and MEIGS, J. V. (1948). Menstrual dysfunction due to emotional factors. *American Journal of Obstetrics and Gynecology*, **55**, 1037-1043.

HAESUNGCHARERN, A. and CHULAVATNATOL, M. (1973). Stimulation of human spermatozoal motility by caffeine. *Fertility and Sterility*, **24**, 662-665.

LANGER, G., LEMBERG, E. and SHARF, M. (1969). Artificial insemination. A study of 156 successful cases. *International Journal of Fertility*, **14**, 232-240.

MARSHALL, J. (1968). Congenital defects and the age of spermatozoa. *International Journal of Fertility*, **13**, 110-120.

PENNINGTON, G. W., BEAZLEY, J. M. and WILSON, E. W. (197[illegible]). Ovulation: its detection and evaluation using multiple criteria in the infertile woman. *Journal of Obstetrics and Gynaecology of the British Commonwealth*, **77**, 627-633.

PEYSER, M. R., AYALON, D., HARELL, A., TOAFF, R. and CORDOVA, T. (1973). Stress induced delay of ovulation. *Obstetrics and Gynecology*, **42**, 667-671.

PORTNOY, L. (1956). Artificial insemination (A.I.D.). Experiences with its use in eighty barren marriages. *Fertility and Sterility*, **7**, 327-340.

SCHOENFELD, C., AMELAR, R. D. and DUBIN, L. (1973). Stimulation of ejaculated human spermatozoa by caffeine. *Fertility and Sterility*, **24**, 772-775.

SCHOENFELD, C., AMELAR, R. D. and DUBIN, L. (1975). Stimulation of ejaculated human spermatozoa by caffeine. *Fertility and Sterility*, **26**, 158-161.

SEYMOUR, F. I. and KOERNER, A. (1941). Artificial insemination present status in the United States as shown by a recent survey. *Journal of the American Medical Association*, **116**, 2747-2749.

STEINBERGER, E. and SMITH, K. D. (1973). Artificial insemination with fresh or frozen semen. *Journal of the American Medical Association*, **223**, 778-783.

STURGIS, S. H. (1962). *The Gynecological Patient—a Psychoendocrine Study*. New York: Grune and Stratton.

The Author

Robert G. D. Newill, MD, MRCGP, Clinical Assistant.

ABSTRACTS OF THE PROCEEDINGS OF THE UROLOGICAL SOCIETY OF AUSTRALASIA

28th ANNUAL GENERAL MEETING, SYDNEY, 1975

President: B. S. PEARSON (Sydney)
Honorary Secretary: H. THOMAS (Sydney)
Editor: G. F. MURNAGHAN (Sydney)

Trauma to the Urinary Tract

By PROFESSOR HANS MARBERGER
University of Innsbruck, Austria

With the increase in traffic, industrial and sport accidents, there is a parallel increase in the trauma of the urogenital tract. In our hospital we observed that in every 4th case of abdominal trauma the upper urinary tract was also affected and in 10% of patients with pelvic fractures the lower urinary tract was also seriously injured. Moreover, almost one-third of patients suffered from temporary or permanent functional disorder of the genito-urinary tract. Involvement of the genito-urinary tract in the polytraumatised patient means a most serious complication with a considerable increase in the risk of injury.

Rupture of the kidney is the most impressive and dangerous traumatic lesion. Diagnosis is simple, by consideration of history, physical examination and excretory pyelography which confirm the diagnosis and yield enough information to indicate emergency operation. Renal angiography may give valuable further information and may clarify reparable traumatic damage of the renal vessels. Therapy of major renal injuries comprises exploration of the severed kidney, evacuation of haematoma, inspection and haemostasis as necessary. Badly damaged parts are removed but vital parenchyma is preserved and any wound in the kidney is repaired surgically. Effective drainage of the perirenal area is allowed for in closure of the incision. There is the possibility of subsequent hypertension from preservation of poorly vascularised renal tissue.

Traumatic lesions of the ureters are mainly iatrogenic.

In this experience the urinary bladder was less frequently injured than the urethra and usually as a result of pelvic fracture and seldom from bursting injury through direct action of violence. Though rupture of the bladder causes typical symptoms, this injury tends to be overlooked in the polytraumatised patient unless it is specifically looked for. Pyelography and urethrocystography comprise emergency diagnostic measures and emergency treatment consists in suprapubic incision with surgical treatment of the bladder lesion and drainage of the perivesical space.

Injuries of the urethra are a most controversial subject in respect of diagnosis and therapy. They occur most frequently as a result of pelvic fractures or straddle injuries. Bleeding from the urethra, together with disturbances of micturition following pelvic trauma, demand urological examination. The clinical assessment with pyelography and urethrocystography do not only allow for diagnosis of the injury but also indicate location and severity. Both conservative and aggressive treatment of urethral injuries have yielded good results when properly applied. We tend towards a more aggressive plan of treatment. With demonstrable lesions of a certain size and symptomatology, suprapubic cystostomy for urinary deviation should at least be applied. Major distortion of urethral stumps indicates immediate repair by suprapubic or perineal approach with evacuation of haematoma, approximation of urethra fragments over a splint and drainage of the wound and bladder. Stabilisation of the severed pelvis is recommended.

The external genitalia form a common site of injury from either sport or work. The treatment varies from case to case but the danger of these injuries should not be underrated.

The Management of Urethral Injury

By R. F. MCILROY, FRCS, FRACS
Auckland Hospital, New Zealand

Traumatic rupture of the urethra is an uncommon accident but its initial treatment determines subsequent prognosis. The development of a stricture results in severe morbidity.

Diagnosis should be made on the clinical triad of blood at the urethral meatus, inability to pass urine and subsequent retention of urine. The absence of a palpable prostate on rectal examination is usually the sign of a large pelvic haematoma rather than complete disruption of the urethra with dislocation of the prostate.

Urethral catheterisation is contra-indicated as an aid to diagnosis. The trauma of catheterisation may convert an incomplete rupture to a complete rupture and infection may be introduced into the surrounding haematoma with promotion of subsequent stricture formation.

During 1972 and 1973 a series of 11 patients were treated for urethral injury and of these 3 had haematuria but were able to void spontaneously, 3 had rupture of the membranous urethra and 5 had injuries to the bulbous urethra. Suprapubic cystostomy was carried out on the 8 patients who were unable to void and voiding urethrograms were taken at intervals from 4 to 14 days thereafter. These studies showed that in the group of 5 patients with injury to the membranous urethra, the urethra was intact in 2, had undergone partial rupture in 1 and complete rupture in 2 patients. The intact urethras allowed for spontaneous voiding, the partial rupture healed after suprapubic bladder drainage without evidence of subsequent stricture formation. The complete ruptures were treated by 2-stage urethroplasty without evidence of subsequent stricture.

3 patients sustained injury to the bulbous urethra with partial rupture in 1 patient which healed spontaneously within 2 weeks but with complete rupture in the other 2 patients and these required surgical repair.

Conservative management of urethral injury by suprapubic cystostomy gives good results but will not prevent formation of urethral stricture which must surely result from complete rupture of the urethra. Suprapubic urinary drainage does, however, allow for definitive operation to be performed upon the urethra at a time when the local tissue haematoma and oedema has subsided and when the general condition of the patient is optimal for prolonged general anaesthesia. When there is only partial rupture of the urethra then suprapubic cystostomy avoids the risk of trauma to the remaining intact urethral mucosa and the further risk of stricture formation.

If rupture of the urethra is suspected on the clinical signs of blood presenting at the external meatus, inability to pass urine and subsequent retention, then suprapubic cystostomy should be performed. Voiding cysto-urethrography can be carried out some 5 to 7 days later and if complete rupture of the urethra is demonstrated then reconstructive surgery can be undertaken 4 to 6 weeks later.

A One-stage Repair of Urethral Stricture

By P. HARBISON, FRCS, FRACS
The Queen Elizabeth Hospital, Adelaide,
South Australia

Urethral strictures are commonly repaired by 2-stage operations with an interval of 3 to 4 months between stages. Recent progress in urethral surgery has tended towards 1-stage repair using either pedicle flaps or skin grafts. The single stage procedure using a skin pedicle flap with a broad anterior scrotal base has been used in the management of urethral stricture in each of 6 patients.

After exposure of the stricture through a large, broad-based incision a pedicle graft is developed with a transverse incision in the scrotum, anterior to the flap used to expose the stricture. This pedicle may be from 2 to 6 cm long so that any length of urethra can be replaced. The pedicle is developed on a broad vascular flap and sutured over an indwelling catheter to fill the defect of the excised urethral stricture. The pedicle has been maintained in position by dexon sutures and urethral or suprapubic urinary drainage has been used for approximately 2 weeks. Satisfactory results of this procedure have been obtained in the series of 6 patients with a follow-up period up to 18 months.

The Urological Complications of Gynaecological Cancer Treatment

By ASHTON MILLER, MD, FRCS
The Norwegian Radium Hospital, Oslo

During the 5-year period from 1970 to 1974 over 4,000 cases of gynaecological cancer were treated at the Norwegian Radium Hospital. Standardised schemes of treatment were used after classification according to the system advocated by the International Federation of Obstetrics and Gynaecology.

Complications related to cancer infiltration, urinary infection, surgical injury to the ureter and the bladder and the effects of radiotherapy.

In respect of cancer infiltration, all cases were investigated by cystography and urography before staging and in the case of stages I and II cancer of the cervix, both preoperative and peroperative lymphography were performed. Anuria due to bilateral ureteric obstruction by tumour may be treated by ureterostomy *in situ* but it is stressed that there is a difference in management between uraemia due to primary tumour and that due to recurrence of tumour.

Urinary infection is associated with indwelling urethral catheter drainage during the period when radium is implanted in the vagina or cervix. With careful prophylaxis and management the short and long-term complications of infection are few, pyelonephritis being rare and urethral stricture more frequent. Postoperative urography has been performed as a routine after hysterectomy in evaluation of possible surgical injury of ureter or bladder.

Irradiation injuries have provided the most difficult problem because normal healing mechanisms are disturbed to such an extent that ordinary surgical methods have no application and tend to result in a worse situation, with particular limitations and increased operative risk of operations within the irradiated field more than 3 months after irradiation. The basic question as to whether or not residual cancer is present has considerable influence upon any decision concerning treatment.

Reconstructive Surgery in Exstrophy of the Bladder

By G. F. MURNAGHAN, MD, CHM, FRCS
A. C. BOWRING, FRCS, FRACS
A. D. PELLY, FRCS, FRACS

In each of a series of 14 patients primary reconstruction of the bladder in exstrophy has been carried out 1 week after bilateral iliac osteotomy. In all but 1 patient these procedures were carried out between the ages of 5 months and 20 months and usually about the age of 1 year. There were 5 females and 9 males, including 2 male patients with complete epispadias. None of these patients have achieved significant continence but 2 of them are dry (1 female and 1 male), lying supine and perfectly relaxed but would be wet immediately on assuming ambulation or exertion.

4 of these reconstructions produced remarkably good bladders with capacities between 50 and 80 ml despite the absence of enough urethral resistance to prevent incontinence.

After primary closure vesico-ureteric reflux was detected in 100% of the female patients and 85% of the males. In 80% of the females and 33% of the males, reflux was grade 3 and considered to have a high risk of retarded renal growth and chronic pyelonephritis.

Careful review of bladder capacity and reflux by regular cystography indicated any need for urinary diversion by cutaneous uretero-ileostomy which was undertaken in 3 female and 4 male patients.

In 5 of the remaining 7 patients, including 4 with large-capacity bladders, it was thought reasonable to undertake ureteric re-implantation across the base of the bladder with tubularisation of the trigone to a mucosal calibre of 10F and with muscular reinforcement of the new "bladder neck". After such secondary reconstruction 1 girl, aged 3 years, is continent of urine up to 3 hours by day with indication of desire to void and with micturition which produces a good urinary stream without vesico-ureteric reflux and leaves an insignificant residuum. Another girl at the age of 4 years has complete urinary control by day, but with imperfect control at night. 2 boys during their first year of follow-up have maintained satisfactory renal growth and drainage from the upper urinary tract but their urinary control remains imperfect and is unlikely to improve significantly. In the 5th patient secondary reconstruction included nipple reimplantation of the ureters which prevented vesico-ureteric reflux but there was retraction of the nipples with some stenosis and upper urinary tract damage requiring relief by urinary diversion.

Penile reconstruction has been undertaken successfully in 4 boys, in whom the epispadias was left complete at the time of closure of the bladder with reconstitution of the bladder neck. Reconstruction required mobilisation of the full thickness of penile urethra as a dorsal strip which could be rolled into a tube which was passed downwards through an incision separating the roots of corpora cavernosa so that the urethra presented as a peno-scrotal hypospadias. After approximation of the 2 halves of the bifid glans and distal corpora, the prepuce was detached from the corona, split and buttonholed for the glans to protude and for the prepuce to supply skin cover to the dorsum of the penis. Adequate mobilisation of the penis during this procedure requires excision of all the scar tissue in the pubic and suprapubic regions with division of the bifid suspensory ligament of the penis. Good skin cover has been obtained by Lindberg advancement of abdominal wall skin. In the oldest boy of this series the hypospadias opening has been advanced to the glans by a Cecil procedure.

The Upper Urinary Tract in Urethral Valves

By W. L. F. UTLEY, FRACS
Christchurch, New Zealand

Children with urethral valves who present after the age of 3 years usually require resection of the urethral valves alone to restore normal function and to relieve progressive damage to the upper urinary tract. However, cases presenting in infancy are more difficult to deal with because removal of the primary obstruction caused by urethral valves is more difficult technically when the infant is only a few days old. In such cases bilateral nephrostomy is carried out and when subsequent ureterograms show no obstruction at the lower ends of the ureters then the valves are resected at 6 weeks of age and nephrostomy tubes are removed. The results of this programme are reasonably satisfactory.

In those cases where there is impaired drainage through the lower ends of the ureters, whether this be due to achalasia or ureteric atony, then the long term results are very unsatisfactory. 6 such cases were treated by terminal cutaneous ureterostomy drainage with reimplantation of the ureters into the bladder some 12 to 18 months later; these children failed to thrive with progressive impairment of renal function in association with gross vesico-ureteric reflux and required further treatment with urinary diversion by cutaneous uretero-ileostomy.

It is conjectured that such urinary diversion should be the treatment of choice in those cases where there is a hold-up of drainage from the ureters into the bladder.

Re-implantation of the Ureter

By P. CLARK, MA, MD, MCHIR, FRCS
R. U. HOSMANE, FRCS
General Infirmary and St James's Hospital,
Leeds, England

The results of re-implantation of 91 ureters in a series of 56 patients over a 10-year period with a mean follow-up period of 4 years have been reviewed. The analysis suggested that: 1. The aim of re-implantation should be to restore the passive mechanism which prevents reflux; 2. A combined extravesical and intravesical approach has many advantages; 3. Preservation of the lower end of the ureter has many advantages and excision is unnecessary; 4. Re-implantation in the presence of a raised blood urea level is probably worth while; 5. Re-implantation of the ureter is a satisfactory operation with few immediate or late complications.

Ureteric Trauma

By R. B. BROWN, FRCS, FRACS
Alfred Hospital, Prahran, Victoria

The clinical management of ureteric trauma has been influenced by the results of a series of 52 experiments to evaluate the healing processes of dog ureter. These studies illustrated the importance of proximal urinary diversion before epithelial apposition and the advantages of efficient splintage in preventing excessive scarring. Muscle regeneration as the site of injury was minimal in almost all experiments.

In a clinical series of 44 cases of ureteric trauma, gynaecological injuries were causative in 20, other surgical injuries in 21 and external penetrating or non-penetrating trauma in 3 cases.

Specific treatment resulted in 54 operations including 18 nephrectomies (12 primary, 6 secondary), 15 uretero-neocystostomies, 8 primary or secondary ureteric anastomoses, 3 uretero-ureterostomies and 3 retrograde ureteric catheter drainage procedures. 3 seriously ill patients required primary nephrostomy or ureterostomy and 2 required primary abscess drainage. 1 patient was managed by ureteric replacement with ileum and 1 by uretero-ileoneocystostomy.

Delayed lower ureteric injuries provided the largest group in the series and the majority of these were treated by uretero-neocystostomy. Delayed upper ureteric injuries produced the poorest results because of the post-traumatic scarring of the ureter and lack of renal and ureteric mobility. Ureteric ligation is condemned because of the risk of septicaemia. Silastic material has been found most advantageous for splintage and nephrostomy drainage.

Prognosis depended largely upon the type and site of injury and upon the duration of delay between injury and treatment. 89% of the cases in this series were diagnosed after the 4th day subsequent to injury.

Ureteric repair was regraded as satisfactory in the absence of urinary tract infection if the postoperative excretory urogram was normal or showed only minimal proximal dilatation.

14% of the attempted repair operations were failures, 20% did not satisfy the criteria for success, thus leaving an overall success rate of 66%.

The Behaviour of the Ureters following Wertheim Hysterectomy and Radiotherapy for Carcinoma of the Cervix Uteri

By J. STUART TAYLOR, FRCS, FRACS

Royal Newcastle Hospital, Newcastle, N.S.W.

The behaviour of the ureters following Wertheim hysterectomy and radiotherapy for carcinoma of the cervix uteri has been studied in a series of 19 patients. Each patient was subjected to physical examination including rectal palpation, intravenous urography with cine screening, and Franzen needle biopsy of any lesion which was suspicious of tumour recurrence.

The usual pattern of behaviour of the ureters is for slight to moderate dilatation to develop down to a level just below the sacro-iliac joint, with normal calibre ureter below this. This lower section of normal calibre ureter appears to correspond with that portion of the ureter which had been stripped clean at the Wertheim operation. The ureteric dilatation is usually bilateral and in the majority of cases commences within a week of the operation and has disappeared at the end of 6 months. The ureteric dynamics appear normal. Dilatation of the ureter following Wertheim hysterectomy and radiotherapy is of no value as a means of determining whether recurrence of tumour is present or not; this series included some cases with ureteric dilatation without recurrence and others in which recurrence of tumour was present but the intravenous urogram was normal. In this context rectal palpation was of very great value; the usual normal findings of a smooth fan of tissue is replaced by irregularity or mass formation when tumour recurrence appears. Transrectal Franzen needle aspiration biopsy was found to be of value in determining whether recurrence had occurred. The cytological findings correlated exactly with histological and post-mortem findings and no false positive or false negative results were obtained.

In Situ Carcinoma of the Urinary Bladder

By JOHN SWINNEY, MC, MD, MS, FRCS

Busselton, Western Australia

Attention was first drawn to the occurrence of carcinoma *in situ* in the urinary bladder in 1952, when it was described as a raised, red velvety patch as seen through the cystoscope. Such an area is circumscribed with normal intervening mucosa so that it should not be mistaken for patchy cystitis. It has since been shown that carcinoma *in situ* may occur in mucosa which looks normal at cystoscopy and is associated with proliferative tumours of the bladder in a high proportion of cases; other changes short of carcinoma *in situ* but regarded as pre-cancerous may also be present when proliferative and invasive growths are seen. Similar changes occur in the ureteral and urethral mucosae in one-third of all cases of bladder cancer and in association with urothelial tumours of the renal pelvis and ureter.

It seems likely that these changes are the result of the action of carcinogenic substances excreted in the urine and form the background to the occurrence of proliferative tumours. The treatment of such growths alone, without reference to the associated generalised mucosal changes, probably accounts for the recurrence of bladder tumours after local treatment, especially when they, as they often do, recur in another part of the bladder to the site of the original tumour.

Some workers recommend radical cystectomy when carcinoma *in situ* is found, but this seems unnecessarily aggressive when the lesions may remain unchanged for years before becoming invasive, yet close follow-up is essential to guard against this eventuality. Radiotherapy has little effect on intra-epithelial cancer but it is believed that after endoscopic resection of a bladder tumour when multiple blind biopsies of the intervening mucosa show pre-cancer or carcinoma *in situ*, then steps should be taken to treat the affected mucosa also. Of available methods, intra-cavitary chemotherapy seems to be helpful and Thiotepa is the most effective agent instilled once a month as a prophylactic between follow-up cystoscopic examinations and until the lesions resolve. Local hyperthemia to the bladder is probably also effective and is being evaluated.

When radical surgery is undertaken for bladder cancer, preoperative endoscopic and histological assessment of the urethral mucosa is worth while in order to determine the necessity for urethrectomy along with cystectomy. Frozen section histology of the lower ureter at the time of division during cystectomy may help to detect the presence of intra-epithelial cancer in the ureteric mucosa before it is implanted into the intestine for diversion of the urine.

The TNM System of Classification of Carcinoma of the Bladder

By ASHTON MILLER, MD, FRCS

The Norwegian Radium Hospital, Oslo

This project was started 5 years ago as a trial of the TNM preoperative classification system of bladder tumours. Clinical trials were based on the system and designed to test: 1. The effect of Thiotepa instillation on the recurrence rate of non-invasive papilliferous tumours; 2. The relative merits of surgery and radiotherapy in the treatment of carcinoma showing early invasion, Group T_1; 3. The relative merits of surgery combined with radiotherapy compared with radiotherapy alone in the treatment of carcinoma invading muscle; 4. The relative merits of irradiation and irradiation combined with chemotherapy in the treatment of T_4 tumours, *i.e.* those invading tissue out to the pelvic wall or invading other pelvic organs.

The non-invasive T_{IS} group and the advanced T_4 group present little difficulty. The 3 groups which show varying degrees of invasion, T_1, T_2, and T_3, are difficult and underestimation of invasion is usual. Efforts to increase the accuracy of classification by adding pelvic arteriography, foot lymphography, grading of tumour cell differentiation and explorative laparotomy to the basic 4 investigations showed that cystoscopy, biopsy histology, examination under anaesthesia and explorative laparotomy were the only investigations which were consistently useful. Laparotomy is regarded as essential before all kinds of open surgery and should be seriously considered before radical radiotherapy is used in the treatment of early invasive tumours of the bladder.

Conservative Surgical Management of Primary Tumours of the Ureter

By J. W. F. MACKY, FRACS

Auckland Hospital, Auckland, New Zealand

Over the years 1-stage nephro-ureterectomy with excision of a cuff of bladder wall about the ureteric orifice has been advocated for the surgical treatment of primary tumours of the ureter. This policy has been challenged in many centres and electric conservative resection of the ureter has been advised wherever possible. Refinements in diagnosis and a better appreciation of the pathology and natural history of these uncommon tumours should allow more rational treatment of individual lesions.

Prognosis appears to be determined by the grade and stage of tumour rather than by the type of operation carried out. 4 patients with ureteric tumours have been treated by conservative resection; 3 patients were male and had grade 1-2 papillary carcinoma whilst 1 female had an elongated polypoid lesion prolapsing at the ureteric orifice. All have remained symptom-free postoperatively but 1 patient required diathermy treatment for small papillary lesions in the bladder some 6 months after ureteric surgery and another patient developed a contralateral ureteric tumour 6½ years after the primary operation.

Local resection of primary ureteric tumours is indicated without question in cases of overall renal insufficiency, unilateral kidney and congenital anomaly such as a horse-shoe kidney when heminephrectomy is impracticable. Benign tumours, preferably after confirmation by frozen section histology, and especially in the younger age group, are probably best treated by local resection.

Nephro-ureterectomy is indicated when more than 1 or 2 tumours are present, when a proximal tumour cannot be positively excluded, when the ipsilateral kidney is destroyed or when the continuity of the ureter cannot be restored.

A decision may be difficult in the case of locally resected low-grade malignant tumours with demonstrably normal upper urinary tracts but local resection should be considered on the grounds that functioning renal tissue may be conserved and the fact that nephro-ureterectomy does not extend the curative potential of surgery.

Hydrodynamics and Urinary Infection

By PROFESSOR HANS MARBERGER

University of Innsbruck, Austria

Many principal questions in regard to aetiology and pathogenesis of urinary tract infections are still unanswered. The theories usually mentioned in textbooks are not satisfying because they do not consider the basic laws of hydrodynamics and the physiology of the urinary tract.

Therefore, we were looking for a new approach to these problems and found a lead in nature. Although a river bed does not seem to be comparable to a ureter or a bladder outlet, close observation of a stream helps advance the understanding of many problems of pathophysiology in the urinary tract.

Basically the same hydrodynamic laws are effective for the flow of water in the riverbed and the transport of urine in the ureter.

The fact that the extent of self-purification of a river depends on the type of flow brought up the question whether urodynamics and flushing play a similar role in the cleansing of the urinary tract from bacteria. We decided to study this problem and set up a research programme.

Studies were conducted to investigate the hydrodynamic properties of various models simulating the bladder neck and ureter. Flow studies were performed with various fluids and under various conditions.

Flow has been made visible by adding dyes, aluminium dust, milk etc., well-floating corpuscles, which do behave in fluids under certain conditions very similarly to bacteria. In simple experiments we could prove that streamlined glass tubes with good hydrodynamic properties could be cleared much more rapidly from bacteria by perfusion fluid than from non-streamlined kinked tubes of the same minimal diameter and volume.

Our investigations confirmed that hydrodynamic laws rule both water engineering and urological fluid problems. Turbulence interferes not only with flow but also with the elimination of suspended particles. The investigations demonstrated that bacteria are not expelled from a dilated urethra or a ureter properly and subsequently reach a pathological density.

Electrostimulation in the Management of Neurogenic Bladder Disorders

By R. H. FARNSWORTH, FRCS(ED), FRACS

The Prince Henry Hospital, Little Bay, N.S.W.

In spina bifida anomalies with meningomyelocoele there is usually an associated neurogenic bladder disorder. The main urological problems in children so affected are the prevention of progressive renal damage and control of urinary incontinence. If untreated, more than 50% of such patients will develop progressive renal damage and it could be expected that less than 10% would develop socially acceptable urinary control. These results of conservative management have led to the frequent use of urinary diversion by uretero-ileostomy in an attempt to protect the upper urinary tract and to solve the problem of incontinence. Recently, concern has been expressed about the long-term results of such diversion.

Professor Francis Katona from Budapest has developed a technique of electrical stimulation of the bladder which has been applied to the management of neurogenic bladder disorder in spina bifida with reported alteration in the functional behaviour of the bladder so that upper urinary tract protection and virtually normal urinary control have been achieved in 66% of children treated.

In this series the Katona technique of electrostimulation of the bladder has been applied to 15 patients with neurogenic bladder disorder in spina bifida. Each patient was evaluated by cystometry, cystography, electromyelography and urodynamic studies before and after the course of treatment. In all but 3 of the 15 patients significant changes occurred with alteration in detrusor contractility and in the development of bladder sensation. In one-third of the patients these changes in bladder function were marked and well sustained and it is considered that these results are sufficiently encouraging to warrant further evaluation of the technique.

Impotence

By I. Potts, FRACS

Sydney Hospital, Sydney, N.S.W.

The causes of organic impotence relate to interference with neural, hormonal, genital, psychic and neuromuscular factors upon which erection usually depends.

In respect of neural factors, observations in man have mainly been concerned with the results following spinal injury at various levels and these are well documented. There are few reports relating to the influence of cerebral lesions, but it has been noted that temporal lobe lesions may be associated with impotence, whilst libido is retained. Temporal lobectomy may cause temporary impotence, whereas bilateral temporal lobectomy may cause hypersexuality. There would appear to be no localised higher centre for erection or ejaculation in man, such as is present in lower mammals.

Hormonal causes of impotence are infrequent but are well documented and the association may readily be recognised in acromegaly, Addison's disease, hypopituitarism, myxoedema, Cushing's disease, pseudo-hermaphroditism, feminising tumours and hypogonadism. Diabetes mellitus is of more importance because of the greater frequency of occurrence and the greater possibility of this condition being overlooked; approximately 50% of male diabetics are impotent and this incidence is not related to the duration of the diabetes or its severity and there is no effective therapy.

Any lesion which diminishes arterial input will obviously impoverish erectile ability of the penis and impotence may follow aortic-iliac occlusion but may also be associated with generalised small vessel disease.

Interference with peripheral nerve connection may be surgical or pharmacological. Bladder-neck closure may be impeded by either presacral nerve section or alpha receptor blockade by phenoxybenzamine (Dibenyline) so that retrograde ejaculation may occur. Contrariwise it could be prevented by the administration of ephedrine. The full pharmacological effects of antihypertensive drugs are generally appreciated but there are specific drug differences. Both guanethidine (Ismelin) and reserpine inhibit alpha adrenergic receptor activity by depletion of norepinephrine storage at the nerve endings and both produce relaxation of the bladder neck. However, Ismelin interferes with ejaculation whereas this has not been reported with reserpine medication. It is not generally appreciated that other drugs in common usage, such as phenytoin (Dilantin), chlorpromazine (Largactil), also have an alpha adrenergic blocking action. Drugs such as probantheline bromide (Probanthine) which inhibit the action of acetylcholine on structures supplied by postganglionic autonomic nerves may rarely cause impotence.

Though libido remains normal during medication with guanethidine it is reduced in 15 to 20% of patients taking methyldopa (Aldomet). Clonidine hydrochloride (Catapres) has no effect on sexual function apart from a slight depression of libido from the mild sedative action. In this present series 11 patients who were impotent whilst taking methyldopa regained potency when their medication was changed to clonidine hydrochloride. Unrelated drugs such as spironolactone may cause gynaecomastia and impotence through hormonal changes. Digoxin is rarely responsible for gynaecomastia with loss of libido because of hormonal changes. Beta blockade agents may also cause loss of erection and absence of libido in association with a depressogenic effect.

Psychiatric Aspects of Impotence

By R. Vickery, DPM, FANZCP

Royal Prince Alfred Hospital, Sydney, N.S.W.

Assuming that all known organic or pharmacological causes of impotence have been excluded or treated, it is then important to consider "constitutional" factors, as well as "psychogenic" ones.

In recent years there has been a deal of reconciliation between physical and psychological schools and a tendency to regard impotence as psychosomatic. There is less tendency to disregard the normal variation in sexual function, with emphasis on Kinsey's idea of sexual potency as a continuum. Constitutional very low or very high sex drive can rarely be altered significantly by any therapy.

The most frequently asserted "psychogenic" causes of impotence encountered at interview include anxiety and fear, hostility and resentment, disgust, inversion of sex drive, inhibition, personality factors, ignorance and misinformation and functional psychoses—especially schizophrenia and endogenous depression.

Changing social attitudes to sexuality have also led to young men presenting more frequently with impotence, to young women more frequently complaining of the impotence of their lovers and to newly "freed" women demanding sexual performance. This challenge to manhood has led to a common finding, in the last decade, of male concern—"will I have to maintain an erection to maintain a relationship"—instead of the previous simple concern to satisfy the woman. A man's impotence is obvious and women's frigidity can be hidden and the sexual adequacy must be judged within the context of each individual sexual relationship.

Many cases of secondary impotence can be traced to a partner, especially if she is a hysterical personality, or there is evidence of sexual game playing. Resentment and hostility on both sides must be considered both in regard to cause and effect and may only be obvious after prolonged interviews, especially conjoint. Attainment of orgasm and maintained erection have been shown to depend upon increasing excitation, where an important constituent is the excitement coming from the partner.

Psychiatric treatment in the past has not yielded good results, probably because of only seeing the more serious and constitutional cases and because the female partner has not been included somewhere in the treatment programme.

Analytical, non-directive psychotherapy has yielded disappointing results in the past. Directive, didactic interviews, aimed at correcting misconceptions, sex education and spelling out differences in male and female attitudes and expectations, can produce surprising results in young patients.

Behaviour therapy using relaxant drugs, hypnotherapy, teaching relaxation manoeuvres, has shown signs of promising results, especially when combined with intensive psychotherapy in cases where there are associated behaviour disorders, secondary gains from symptoms and troublesome interpersonal relationships. In cases where fear, anxiety or disgust are high, deconditioning therapy has produced, if anything, better short term results than analytical psychotherapy. A proportion of patients will require advice to find another or certain stereotype partner.

It could be argued that too much emphasis is placed upon psychological facets, except in the prophylactic sense of better adolescent and adult sex education. It is to be hoped that developing psychophysiology, and availability of technical innovations such as penile transducers, microcameras, and electronic devices will produce opportunity to study the interrelationships of various psychological states and sexual functioning and especially disordered potency.

Plasma Testosterone in Prostatic Disease

By Professor Hans Marberger

University of Innsbruck, Austria

Experience with plasma testosterone (PT) levels began in 1967 and in the early years the assays were made by the competitive protein binding method, which was later replaced by radioimmunoassay.

Estimation of the normal mean PT level in various age groups has shown that this is extremely low in prepubertal boys but with a rapid increase around the age of 30 years to reach a plateau level at the middle of the 3rd decade. There is a slow decrease in the next 20 years of life with a rapid fall from the 6th decade onwards. Individual variation as represented by the standard deviation is considerable and appears to increase in the older age groups.

PT levels were compared between healthy men and patients with various prostatic diseases in the same age groups but no differences were found. Very low PT levels were found in patients with carcinoma of the prostate during treatment with antiandrogenic therapy. The PT level was regarded as a valuable index in the palliative treatment of prostatic carcinoma. Very low PT levels were also found in a group of 11 patients with purulent prostatitis. The reason was thought to be the reduced general state of health in these patients.

A large series of 100 healthy men were sub-grouped and investigated for levels of PT in 20 subjects, luteinising hormone (LH) in 30 subjects and dihydrotestosterone (DHT) in 50 subjects. The results of these hormone assays were compared with values obtained from a series of patients known to have either benign prostatic hypertrophy or carcinoma of the prostate but no significant differences could be found, though the series was small. DHT levels have shown a trend of difference with increasing number of cases studied and with the same high individual variation as shown by standard deviation in the older patients as was found with PT levels.

From these studies it can be concluded that determination of PT level does not elucidate the aetiology of prostatic disease. PT levels form only one parameter of the endocrinological situation, and do not give information about production rate, turnover or metabolism. It might be more promising to investigate androgen metabolism and action in the prostatic cell. Current research indicates that androgen action may be blocked much more effectively by blocking androgen binding or transport or by blocking the receptor system.

Peyronie's Disease

By A. P. Tynan, FRCS, FRACS

The Prince Henry and The Prince Of Wales
Hospitals, Sydney, N.S.W.

In Peyronie's disease fibrous tissue forms into 1 or more plaques in the tunica albuginea of the penis with possible extensions into the corpora cavernosa with destruction of the bundles of smooth muscle in the septa. This process may be self-limiting and the possibility of spontaneous improvement confuses evaluation of different forms of therapy. Surgical excision of the plaques may be very difficult and necessitate destruction of a large part of the erectile mechanism. It has been suggested that radiotherapy may be helpful in the alleviation of the disease in the early stages and may accelerate the quiescent period.

In this present series 12 patients with Peyronie's disease were referred for radiotherapy. 6 of them had received previous treatment with Potaba, vitamin E, local injection of hydrocortisone and surgical incision in varying combination but without improvement. Ages ranged from 33 to 67 years with a peak incidence during the 4th and 5th decades. 7 of the patients in the series had Dupuytren's contracture. 4 of the total series of 12 patients decided against treatment by radiotherapy and in 2 of these the condition worsened and in 2 it improved. Of the remaining 8 patients, 5 noted definite improvement 1 to 2 months after radiotherapy, with softening of the lesions and diminution of pain. 2 patients developed new plaques some 12 months after completion of radiotherapy.

Though no patients were cured, most of the patients receiving radiotherapy reported a subjective improvement in pain and a possible improvement in other symptoms, to indicate that radiotherapy may possibly shorten the time that this disease takes to become stable.

Surgical Management of Priapism

By J. M. DRUMMOND, FRACS

Royal Prince Alfred Hospital, Sydney, N.S.W.

The pathophysiology of priapism is obscure but there is basically a failure of the normal mechanism which allows for return of the penis to the flaccid state. There is an imbalance between arterial inflow and venous outflow. Most surgical measures have been directed at improving the venous outflow and various shunting procedures have been described including sapheno-cavernosum shunt and caverno-spongiosum shunt.

4 patients presenting with idiopathic priapism have been managed surgically after unsuccessful medical treatment. In 1 patient a sapheno-cavernosum shunt was made but thrombosed after 24 hours. In 3 patients caverno-spongiosum shunt has been successfully applied but despite early relief of priapism only 1 patient is potent. These surgical procedures have been complicated by urethral damage in 1 patient, urethro-cutaneous fistula in another and urethral strictural formation in a third.

LH and PT Release after Stimulation with LH-RH

By PROFESSOR HANS MARBERGER

University of Innsbruck, Austria

It is known that the hypothalamus produces substances which regulate the release of hormones from the anterior pituitary gland. Luteinising hormone—releasing hormone (LH-RH) is one such substance which has been found in hypothalamic tissues in various species including man and controls the release of LH. After this substance was isolated the chemical structure was determined as a decapeptide, it was synthesised and has been administered to normal prepubertal and adult human males. Reports have indicated that this substance is a really efficient hormone in stimulating the gonadotrophic release of LH and follicle stimulating hormone (FSH).

LH-RH has been used as a test for response of the pituitary gonadal axis. Studies have been made of a series of patients including normal prepubertal males and normal adult males, old men with and without prostatic disease and patients with carcinoma of the prostate who have been treated by orchidectomy. After hospitalisation each subject was given 200 μg of LH-RH and plasma testosterone (PT) and LH levels were determined and blood samples taken 10, 20, 30, 60, 120, 180, 240, 480 and 600 min after injection. The PT levels were measured by radioimmunoassay and the LH levels were determined by a modified solid phase radioimmunoassay.

Adult healthy men responded very well to the injection of LH-RH and produced a significant peak of LH 30 min after injection and a peak of PT some 2 hours later. In prepubertal boys LH release was found to be the same as in adults in response to LH-RH injection but there was no increase in the PT levels. Similar findings were observed in cryptorchid boys. There would appear to be a step-wise increase of responsiveness of the gonads to pituitary stimulating hormone in the prepubertal male.

In male patients in the 6th decade without manifest prostatic disease the LH-RH injection produced a significant increase of LH but a lower PT peak in comparison with young males. In some old men no response of Leydig cells was found and in this group the elevated LH levels were considered to represent the beginning of Leydig cell insufficiency, whereby extremely high peaks follow stimulation as the beginning of a negative feed-back mechanism.

Male climacteric seems to start with Leydig cell insufficiency whilst pituitary function is still intact. This assertion has been confirmed by studies on orchidectomised patients in whom LH-RH stimulation causes an excess of gonadotrophin output. PT levels remain unchanged at castration levels.

10 prepubertal boys with unilateral or bilateral cryptorchidism have been given a daily dose of 20 μg i.m. for 2 weeks. In 8 of these 10 patients the testes descended to normal positions and the 2 failures were associated with inguinal herniae and these required repair and orchidopexy.

Treatment of Carcinoma of the Prostate by Continuous Infusion of Stilboestrol Diphosphate (Honvan)

By GRAEME HEAP, FRCS

Canberra Community Hospital, A.C.T.

Stilboestrol diphosphate (Honvan) was developed as a soluble preparation suitable for intravenous administration of oestrogen therapy for carcinoma of the prostate. The efficacy of this drug has been established in several trials but it is usually given slowly as a bolus injection. This method of treatment may be impractical in hospital without resident staff and this trial was undertaken to evaluate the effect of slow continuous intravenous infusion.

Each of 16 patients received a total dose of 10 g of stilboestrol diphosphate over a 10-day period. Each patient was visited once daily and 500 mg of stilboestrol diphosphate was injected into each of 2/500 ml bottles of dextrose-saline. 6·5 mg of thiethylperazine (Torecan) was also added to each bottle for the control of nausea. Each patient was infused with 2 such bottles per 24 hours into a peripheral vein, preferably in the upper limb.

This technique was used in 16 patients who suffered from various combinations of urinary retention and pain. 13 patients improved (80%) as a result of this treatment and of 15 patients with retention 11 improved (75%) and of 7 patients with bone pain and perineal pain 6 were improved (85%).

All of the patients experienced nausea which was controlled by the simultaneous use of a phenothiazine derivative, and phlebitis was common at the site of intravenous infusion and sometimes with local bleeding. Other complications included disorientation, pulmonary embolism, cerebral thrombosis and mild perineal pain; each of these complications occurred once in the series.

Stilboestrol diphosphate appears to soften the fibrous element of the tumour rather than reducing its size and is therefore a useful adjunct to surgery and in 2 patients was thought to be responsible for restoration of micturition when endoscopic resection of the prostate had failed. Though it often has value in the relief of pain it appeared to have little effect in the prolongation of life. In those patients in which stilboestrol diphosphate is successful it usually produces relief within 5 days of commencement.

Hormones and the Kidney

D. J. ELLIS, FRCS, FRACS
Prince Henry's Hospital, Melbourne, Victoria

There are 2 aspects of the relationship between hormones and the kidney which merit consideration, and these relate on the one hand to the types of hormones that may be produced by adenocarcinoma of the kidney and on the other hand to the place which hormones may have in the treatment of patients with extensive adenocarcinoma of renal origin.

Adenocarcinoma of the kidney may produce erythropoietin, parathyroid-like hormone or renin.

About 2·8% of all patients with carcinoma of the kidney manifest polycythaemia which may result from the production of erythropoietin by the tumour of the kidney or its metastases, or possibly from associated ischaemia in adjacent normal tissue. Such polycythaemia will usually disappear with nephrectomy but tends to recur with the development of any metastasis.

Radioimmunoassay has confirmed that adenocarcinoma of the kidney can produce a parathyroid-like hormone to produce all the clinical symptoms of hyperparathyroidism despite the absence of parathyroid disease or evidence of bony secondaries. The symptoms and clinical signs disappear after nephrectomy but tend to recur when metastasis develops.

10 to 20% of patients with adenocarcinoma of the kidney have hypertension. Some renal tumours produce renin but most of these are neoplasms of the juxtaglomerular cells in the form of haemangiopericytoma. There is 1 recorded case suggesting the production of renin by a true adenocarcinoma of the kidney. The possibility of other hormone effects of carcinoma of the kidney are suggested by the association of this tumour with Cushing's syndrome, the nephrotic syndrome, various musculo-skeletal disorders and the metabolic syndromes in the form of pyrexia of uncertain origin, cachexia and liver dysfunction.

Several hormones have been used in the treatment of adenocarcinoma of the kidney. Medroxyprogesterone acetate (Provera) is reported to produce objective improvement in 22% of patients with advancing and extensive carcinoma of the kidney with multiple metastases. Such improvement was usually noted between 2 and 6 weeks and could continue to up to 2 or 3 years with obvious prolongation of life. In 55% of patients there was subjective improvement from Provera with minimal toxic effects which included endocrine and hepatic problems and sometimes vascular degeneration and thrombosis. Testosterone propionate has been used in a number of patients either as initial therapy or following the use of Provera, but this drug has not been very effective. Subjective improvement has been reported in 25% of patients receiving steroid therapy, and in particular prednisolone. Anti-oestrogen compounds are being investigated, synthesised and tested on laboratory animals and tissue cultures and there is significant hope that clinical advances will be forthcoming.

It is apparent that hormones play an important part in the normal clinical course of adenocarcinoma of the kidney and this condition may be associated with a number of different vague and generalised clinical symptoms and signs. The recurrence of such symptoms after apparent surgical cure should be noted as the possible indication of metastases. Laboratory studies based upon tissue culture technique may provide a possible place for laboratory testing of the sensitivity of renal tumours to various hormone preparations. The possibility arises of the use of hormones at an earlier stage in the disease as an adjuvant to and possibly with enhancement of the efficacy of surgery and radiotherapy. The place of combined therapy with hormones and cytotoxics has also to be assessed.

Hormonal Therapy with Steroid-filled Silastic Rubber Implants

BY PROFESSOR HANS MARBERGER
University of Innsbruck, Austria

Steroids diffuse readily through polymethylsiloxan (PDS) membranes (Silastic, Dow Corning Corporation, Michigan, U.S.A.) into various media at a relatively constant low rate. Subcutaneous implantation of PDS capsules filled with dry, crystalline hormone assures a good constancy of hormonal supply to the organism over longer periods of time.

The pharmacokinetical principles of this method of hormone administration have been established in numerous *in vitro* and *in vivo* investigations. A standard PDS capsule has a length of 20 mm, a membrane thickness of 0·8 mm and a surface area of about 150 mm^3. The capsules were filled with dry, milled steroid. The amount of steroid released from the capsule within a certain time depends upon the length, the surface and the thickness of the capsule.

Since 1969 clinical examinations have concentrated upon 3 main fields; therapy of prostatic cancer, substitution in castrated and hypogonadal men and therapy of male infertility.

During a 3-year period the method has been used in the therapy of prostatic carcinoma in more than 100 patients; 2 capsules, each of them containing 22 mg of ethinyl estradiol, have been implanted subcutaneously. Though the time of observation has been too short for clinical and statistical evaluation, it has been found that the disease does not appear to become worse during treatment with PDS capsules.

In the therapy of castrates, or men with severe hypogonadism, testosterone administration by PDS capsules promises to become an ideal solution for the long-term substitution therapy. 1 PDS capsule filled with 22 mg of testosterone releases approximately 55 μg/24 hours at a very low constant rate for about 13 months. This kind of substitute therapy has been used in hypogonadotrophic hypogonadism, in Klinefelter syndromes and in castrates due to bilateral testicular torsion.

Testosterone-filled PDS capsules offer a new possibility of successful treatment of certain forms of male subfertility; in such cases 6 to 10 implants of testosterone have been used.

Clinical results in the human male show good therapeutic response to hormonal treatment by PDS capsules in castrates, hypogonadal and subfertile men. This method of hormone administration has definite advantages over the conventional hormone delivery system including maximal efficacy of the administered hormone, low dosage, reduced expenditure in medical care, simplicity of application and safety without side effects.

had to be replaced because of mechanical failure and this patient is now continent following insertion of a 2nd appliance.

In the final analysis, 5 of 6 patients with the incontinence have been cured by the implantation of a simple device which enables occlusion and opening of the urethra at will.

The device, because of its simplicity both in construction and ease of insertion, is considered to be worthy of extensive trials in post-prostatectomy incontinence and its place in the treatment of neurogenic bladder and possible modification for colostomy control are now under consideration.

A Simple Artificial Sphincter

By M. Rosen, FRCS

Wollongong Hospital, Wollongong, N.S.W.

The device is made of silicone elastomer and provides a mechanism whereby the urethra can be occluded and opened at will. It is intended for use in both sexes and in male subjects may be inserted through a perineal approach and in females either by the retropubic approach or by combined retropubic and vaginal surgery. The device consists of a 3-armed clamp which lies across the urethra in the perineum with 2 arms across one side of the urethra and 1 arm across the other. This single arm carries a balloon which is inflated in order to occlude and compress the urethra. This inflation is accomplished by compression of a bulb which is placed within the scrotum and is connected to the balloon through a narrow tube which is controlled by a valve. Release of the valve allows the bulb to refill from the balloon which deflates and thus enables micturition to commence.

6 patients with urinary incontinence have been treated by this artificial sphincter. The appliance is inserted through a midline perineal incision to expose the urethra, which is immobilised from the urogenital diaphragm so that the 3-pronged clamp may be placed across the urethra with the single arm on the ventral aspect. The tubing and bulb are inserted into the scrotum usually on the right side after dissection to allow for subcutaneous location of the bulb. The wound is closed in layers without drainage and at the end of 1 week the patient is encouraged to manipulate the device by squeezing the bulb to attain continence and releasing the bulb to deflate the balloon in order to allow for voiding.

The ages of the 6 patients ranged from 54 to 82 years and follow-up was from 3 months to 1 year in duration. The incontinence was associated with abdominoperineal resection in 1, endoscopic prostatectomy in 2 and open prostatectomy in 3 patients.

3 patients have been completely cured of their incontinence without complications. The 3 other patients failed to obtain relief and have been re-operated upon. In 1 of these 3 failures the device had to be removed because of sepsis and in another patient the device merely had to be adjusted to provide continence, and in the 3rd case the device

The Surgical Implications of Vascular Anastomoses in the Kidney

By D. L. Rothwell, MB, CHB

Auckland Hospital, Auckland, New Zealand

The presence of collateral vessels to the kidney has been noted both in animals and man with experimental or pathological obstruction to the renal artery.

The main contributions to the perirenal system which comprises the capsular, peripelvic and periureteric arteries are from the lumbar, intercostal, iliac, gonadal and inferior adrenal arteries and the abdominal aorta. The perforating artery connects the intrarenal vessels to the capsular system.

It has been noted that in some cases of total renal artery occlusion, the collaterals may maintain normal renal functions and size by supplying the kidney via the perforating artery.

Not all patients with renal artery stenosis develop collaterals; the reason for this is not known but in those that do develop collaterals it is postulated that the stimulus may come from the renal tissue in the form of a chemical substance.

The collaterals may develop very rapidly, as shown by case reports of embolism occurring in a single renal artery, thus allowing the kidney to be salvaged days after the onset of symptoms.

Autotransplantation is being performed in some centres as a means of establishing normal vascularity in some cases of renal artery stenosis. The results so far seem to be very gratifying and the presence of a well developed collateral circulation may become an indication for autotransplantation as a planned procedure.

In blunt renal trauma it has been suggested that any patient with partial infarction of a kidney and with arteriographic evidence of collateral circulation is best treated conservatively in spite of heavy haematuria; the absence of collaterals in such a situation would be an indication for partial or total nephrectomy as prophylaxis against the subsequent development of hypertension.

The presence of collaterals in renal carcinoma does not necessarily indicate spread beyond the renal capsule. Their presence does, however, provide a good indication for preoperative radiotherapy in order to render the tumour less vascular and to decrease the chances of local metastasis occurring as a result of surgical intervention.

A New Technique for Ferrosilicone Knifeless Nephrectomy or Partial Nephrectomy for Renal Tumours of Unilateral Renal Aetiology Hypertension

By R. D. TURNER, MD, FACS
UCLA School of Medicine, Los Angeles, California, U.S.A.

Open surgery on a kidney is a major surgery which a large number of poor-risk patients cannot survive. A spontaneous autonephrectomy often is a blessing in unilateral renal pathology conditions. A new technique has been devised which obviates the risk involved in renal surgery and can be used under local anaesthesia in a radiology department to block the blood supply to any segment of a kidney or to the entire kidney when desired.

The new technique of transfemoral selective catheterisation of a renal artery and its branches with 2 arterial catheters allows 1 to be used for arteriography and the 2nd for the injection of 2·5 ml of ferrosilicone magnetic molecules to totally fill, obstruct and plug the artery catheterised and all of its branches. A strong electromagnet like a radioisotope renogram head overlying the kidney is used to magnetically pull the "iron filings" ferrosilicone microspheres into the distal arterioles and capillaries. 2½ min after injection the silicone mixed with the iron microspheres solidifies to form a solid "galvanised rubber tree" cast of the entire arterial tree catheterised and this area undergoes immediate necrosis. The tip of the proximal catheter used to do the arteriograms before, during and after the ferrosilicone injection is left in the mid-renal artery whilst a 2nd catheter is selectively advanced into the main branch of the artery supplying the renal segment selected for infarction and necrosis.

Ferrosilicone is non-toxic. If very direct local radiation therapy is indicated then a radioactive isotope such as P32 can be added to the ferrosilicone before its injection through the transfemoral arterial catheter into the kidney.

If a patient has a unilateral renal hypertension aetiology (Goldblatt kidney) or renal artery stenosis then the main renal artery can be obstructed, resulting in essentially a non-surgical nephrectomy. If there is a hypernephroma in 1 kidney, in a poor-risk patient, the ferrosilicone obstruction of the main renal artery will accomplish the non-surgical nephrectomy. In a solitary kidney with a hypernephroma a segmental partial nephrectomy by ferrosilicone necrosis can be accomplished by selective catheterisation of that main renal arterial branch which supplies the tumour-bearing segments.

This technique presents an exciting new frontier in the care of unilateral renal pathological entities.

Idiopathic Cyclical Oedema

By G. D. BURFIELD, FRCS, FRACS
Adelaide, South Australia

Idiopathic cyclical oedema is a clinical syndrome which occurs almost exclusively in adult women. It is characterised by bouts of swelling of the legs and abdominal distension associated with headache, increased irritability and depression. The patients are commonly hypertensive and some have severe nocturnal polyuria. It has recently been reported that certain cases suffering from this syndrome have excessive mobility of the kidneys and can be cured by nephropexy. It is postulated that abnormal mobility of the kidney or kidneys may cause renal ischaemia as a result of stretching or kinking of the renal artery when in the erect position. This leads to decreased renal perfusion with elevated angiotensin levels and hypertension as a consequence. Sodium and water retention leading to oedema may result from diminished filtration of sodium and an increased proportionate absorption of the filtered load. Elevated secretions of aldosterone, secondary to the high angiotensin levels, may also increase sodium retention. 2 cases presenting with the syndrome have been operated upon with clinical success.

Antegrade Pyelography

By J. SAALFELD, FRCS, FRACS
Royal North Shore Hospital, Sydney, N.S.W.

Pyelograms can be made by percutaneous needle puncture of the renal pelvis and injection of urographic contrast material after aspiration of urine. Such antegrade pyelography is useful in selected cases of hydronephrosis which are not adequately diagnosed by usual methods.

Posterior needle puncture of the renal pelvis is relatively simple in large hydronephroses for which it should be reserved. Plain X-ray of the renal tract should be taken, and intravenous and retrograde pyelography should both be attempted with evaluation of renal size, shaping and position prior to attempting antegrade pyelography. Using a 21-gauge lumbar puncture needle the optimum point of puncture is below the 12th rib, 6 cm from the midline, at a level where a 13th rib might lie. Entry into the renal pelvis can be identified by respiratory movement of the needle and by the aspiration of urine which can be examined. 20 ml of urine should be aspirated but the volume of contrast agent injected is always less than that of the urine aspirated. Methylene blue may be added to the contrast and may aid the identification of ectopic ureteric termination or fistula. There are no vital structures between the lumbar skin and the renal pelvis and no major complications have occurred as the result of needling. This technique has been found useful in the evaluation of young patients with hydronephrotic dilatation of the upper polar component of renal duplication. In adult patients it has been used to define the size and site of urinary fistula following radical cystectomy and uretero-sigmoidostomy, or following abdominal hysterectomy for carcinoma of the cervix. The site of ureteric obstruction has been defined by this technique in patients with ureteric stricture after uretero-ileal anastomosis, in idiopathic uretero-pelvic obstruction with pyonephrosis and in ureteric obstruction from carcinoma of the cervix.

Pull-Through Ureterolithotomy

By D. URQUHART-HAY, FRCS, FRACS
Wellington Hospital, Wellington, New Zealand

The removal of a stone impacted in the lowermost end of the ureter can be a difficult surgical procedure.

An extraperitoneal approach to the ureter, particularly in a fat person with a deep and narrow pelvis, may involve a difficult dissection, while transvesical and per urethral approaches through the ureteric orifice may lead to a loss of vesico-ureteric competence. A "pull-through" method has been devised whereby the ureter is dissected from within the bladder and pulled into the bladder to allow for removal of the stone through a small incision made in the ureter over the stone. The ureteric defect is closed and the ureter itself replaced in its original position. There is no interference with ureteric vitality and uretero-vesical competence is maintained.

This method was previously described by Maynard and Landsteiner (1972) and was developed by the author, without knowledge of their work. It has been used successfully on 4 patients, each with a small stone impacted at the lower end of the ureter. It has been found to be a safe and simple procedure and useful in those patients who are obese and in whom the pelvis is deep and narrow.

Reference

Maynard, J. F. and Landsteiner, E. K. (1972). Pull-through ureterolithotomy, *Journal of Urology*, **107**, 365-368.

Renal Transplantation

J. Rogers, FRACS

Royal Prince Alfred Hospital, Sydney, N.S.W.

From the Registry of Renal Transplantation in Australasia it is reported that there have been 1,560 patients treated by 1,750 transplant operations using cadaver donors. In this series 997 patients (64%) are alive and well and 857 (57%) are alive with functioning grafts. Since 1970, when effective tissue typing was introduced, 23 patients have received kidney grafts from live donors and in this smaller group 18 (83%) are alive and well with functioning grafts.

More particular analysis of the results obtained from the Sydney Hospital-Royal Prince Alfred Hospital group show that the main improvement in results has been due to the use of antilymphocyte globulin in addition to standard methods of immunosuppression. Analysis of tissue typing shows that there is a statistically significant improvement in results in the better matched groups as compared with the poorly matched groups: this improvement, although significant, does not justify the wastage of the large number of kidneys which were poorly matched with the recipients. In this local series hyperacute rejection was virtually non-existent and this was thought to be due to the exclusion of patients from transplantation with antibodies detected in a direct cross-matching. The Rosette Inhibition Test was evaluated in a small group of patients and was found to show the greatest promise for the early detection of episodes of graft rejection.

Renal Preservation for Transplantation, or Bench Surgery of the Kidney

By J. M. Drummond, FRCS

Royal Prince Alfred Hospital, Sydney, N.S.W.

Machine preservation was introduced into the Sydney Transplantation Group in January 1973, using a Mox 100 Waters Preservation System with a maximum capacity for 4 kidneys at any one time. Kidneys are perfused with pulsatile flow of a perfusion mixture which is basically a 5% albumin solution with additives and used at 6^{0} to 8^{0}C. Flow rates vary within the range 100 to 300 ml per min and a membrane oxygenator maintains oxygen tension between 150 and 300 mm Hg.

Early in the series a technical problem caused arterial thrombosis in 5 kidneys in association with intimal damage where the tip of the perfusion cannula lay within the renal artery. This complication was subsequently avoided by the *en-bloc* removal of the cadaver kidneys with cannulation of the aorta. An alternative technique uses cannulation of a fresh or freeze-dried common iliac artery segment which is anastomosed to the renal artery and excised prior to implantation of the kidney.

The immediate function and graft survival have been compared between a series of 107 machine-perfused kidneys and a series of 74 non-perfused kidneys. During a 15-month period machine-perfused kidneys gave a graft survival of 64% in comparison with a survival of 59% in the non-perfused group. Immediate function was obtained in 60% of machine-perfused kidneys as compared with 59% in the non-perfused group.

Book Reviews

Urethral Obstruction in Boys. Diagnosis and Treatment of Congenital Value of the Posterior Urethra. By CARL CORNIL. Pp. vi+158 with 26 illustrations. Amsterdam: Excerpta Medica. 1975. £9·28.

No less than 201 boys with congenital valves of the posterior urethra were treated in the Rotterdam urology services in the 5-year period from January 1969 to December 1973 and this book comprises a detailed survey of 150 who had "unquestionable valvular obstruction". It does not explain what the others had.

If ever there was a book for which the aphorism concerning wood and trees was appropriate it is this one. There is a mass of information but it is poorly laid out and it is impossible to discern the important features of the condition under discussion. The first 35 pages are devoted to a description of the familiar clinical, radiographic and endoscopic features of posterior urethral valves and the remaining pages to the "case material". The author has chosen to subdivide each aspect of the cases according to the symptom groupings, which is unfortunate because it leads to confusion, repetition and uninteresting reading.

There is no doubt that a great deal of work has gone into compiling the data which form the core of the book and it is a pity that it is not presented in a more stimulating fashion, particularly as the author's style is pleasant. There is an inescapable feeling that there ought to be a message somewhere but the reviewer could not detect it. As a comprehensive review of the bibliography of a particular congenital abnormality, the book will no doubt be useful, but the price is high and there are other sources which are equally valuable at lower cost.

J. E. S. S.

Pediatric Nephrology. Vol 1. Edited by JOSE STRAUSS, M.D. Pp. 474 with 111 illustrations. New York: Stratton Intercontinental Medical Book Corporation. 1974. $19.95.

This book is a collection of seminars given by various specialists in the field at a conference held in Miami under the chairmanship of the editor. This origin is turned to advantage by the inclusion of discussion sessions which serve to give a balanced view of most issues, thus the overenthusiasm of Dr Richard in stating that routine screening for bacteriuria in children is "mandatory" leads to discussion which makes it clear that screening is not justified by currently available evidence.

This type of book also allows recruitment of chapter authors of great experience. In particular, I found the chapters written by Dr Renée Habib on glomerulonephritis, renal dysplasia and nephronophthisis excellent and I suspect that they will be referred to many times over the next few years.

It is perhaps unfair to single out Dr Habib's contribution since most of the chapters were excellent, but her reports being in general based on a vast personal experience in Paris have authority and permanence. It is difficult to criticise the recommendation of reserpine for the treatment of hypertension since reports of its possible carcinogenic effects came after the date of the conference.

Many would disagree, however, with the relegation of alphamethyldopa to short-term use and the preference for guanethidine in long-term treatment of hypertension. The advice from Dr Vanderwerf that splenectomy may be indicated for leucopenia, although representing one school of thought, should be tempered with a warning of the reported increase in mortality following transplant in splenectomised patients.

One criticism of the arrangement of the book chapters is the opening with a report of the workshop discussions; although excellent it should be read after the rest of the book has been digested since much of the discussion would be meaningless to the non-nephrologist who had not read the other chapters.

Overall the book is authoritative, well illustrated and easily read and is to be thoroughly recommended to nephrologists and urologists with either paediatric or adult interests and to paediatricians in general.

R. W.

Normal and Abnormal Growth of the Prostate. Edited by M. GOLAND (Proceedings of a Symposium at the Southwest Foundation for Research and Education, San Antonio, Texas, March 1973), Pp. 941. Springfield, Illinois: Thomas. 1975. $48.75.

This book does not reveal why the prostate becomes hypertrophied nor does it clarify the problems and doubts that surround the management of carcinoma of the prostate. It is, however, a full report of an international symposium at which almost all current prostatic research was presented; it is clear that much progress is being made towards an answer to these clinical problems. The main emphasis is on the metabolism of steroids and their regulation in the prostate. There is a short section in experimental and clinical approaches to prostatic cancer. It is inevitable, with the delay in publication, that much new work, especially on androgen receptor proteins, has since been reported. Nevertheless, this book represents the best current reference on prostatic research.

G. D. C.

Book Received

Advances in Voluntary Sterilisation. Proceedings of the 2nd International Conference, Geneva, 1673. Edited by M. E. SCHIMA and others. Amsterdam, Excerpta Medica. 1974. Abt. £12·00.

Announcements

THE BRITISH ASSOCIATION OF UROLOGICAL SURGEONS

At The Royal College of Surgeons, 35/43 Lincoln's Inn Fields, London, WC2A 3PN

President: Mr R. A. Mogg, VRD, MCh, FRCS

ANNUAL MEETING 1976 with the CANADIAN UROLOGICAL ASSOCIATION—*Preliminary Programme*

The Annual Meeting will be held in conjunction with the Canadian Urological Association, at the Royal College of Surgeons of England, London on Wednesday, Thursday and Friday, 23, 24 and 25 June. A full programme will be circulated later, but the provisional arrangements are as follows:

TUESDAY, 22 JUNE

2.00-4.00 p.m.	Registration for Canadians *only*.
4.00 p.m.	Address by the President of the Royal College of Surgeons followed by a talk by members of the College staff on "The History of the Royal College of Surgeons".
5.00 p.m.	Tea
5.30 p.m.	Clifford Morson Lecture.
Evening	Private Dinner Parties to be held in the homes of Council Officers for their Canadian colleagues

WEDNESDAY, 23 JUNE

Morning	8.30 a.m.	Registration.
	10.00 a.m.	Topic discussion: "Carcinoma of the Bladder".
Afternoon	2.00-4.00 p.m.	Short Papers.
Evening		Joint Presidents' Reception at the Royal College of Surgeons. Dinner for Executive Committees at the Apothecaries Hall.

THURSDAY, 24 JUNE

Morning	Short Papers.
Afternoon	Topic discussion: "Stone Production".
Evening	Annual Dinner to be held at the Connaught Rooms.

FRIDAY, 25 JUNE

Morning	Short Papers.
12.15 p.m.	Annual General Meeting.
Afternoon	Paediatric Urology Session.
Evening	Reception given by the Canadians for their British counterparts.

SATURDAY, 26 JUNE

All day	Visits to Oxford and Cambridge—programme for Canadian members.

Ladies' Programme

An extensive Ladies' Programme will be arranged and details of this will follow at a later date.

Hotel Accommodation

Members are asked to arrange their own accommodation, but they are advised to make their reservations as soon as possible in view of excessive demands on hotel accommodation in London at this time.

Nominations for Council

The attention of members is drawn to the following Rule:

> "Candidates for the Full Member representatives on the Council shall be nominated by two Full Members at least six weeks before the Annual General Meeting, and shall give their written consent to stand. Candidates for the Associate Member representatives on Council shall be nominated by two Associate Members at least six weeks before the Annual General Meeting, and shall give their written consent to stand."

Three Full Members and one Associate Member will be retiring in 1975 and nominations for the vacancies must be sent to the Honorary Secretary **not later than 16 May, 1976.**

E. CHARLTON EDWARDS
Honorary Secretary

THE BRITISH ASSOCIATION FOR PAEDIATRIC NEPHROLOGY

The Spring Meeting of the Association will take place at York University on Wednesday, 7 April, 1976. The *Windermere Lecture* will be given on that day at 12 noon by Lars Hanson on "The role of *E. coli* infections of childhood".

00 mm

If this page were wider Squibb could have shown the actual size of their new 200 mm x 200 mm (8″x8″)

STOMAHESIVE

Whilst in most cases the regular size Stomahesive has proved entirely adequate, in response to requests from nurses we have introduced the new, larger size. This has been specially prepared for the protection of large perifistular or peristomal skin areas where particularly difficult problems exist.

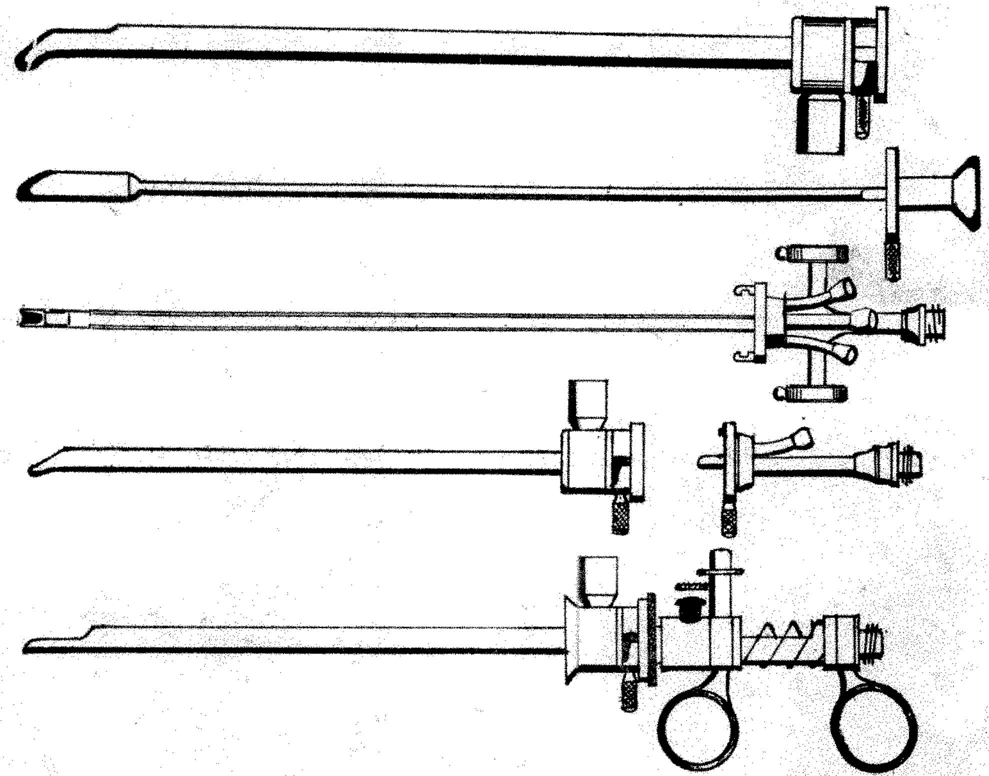
Use Stomahesive-right from the start.

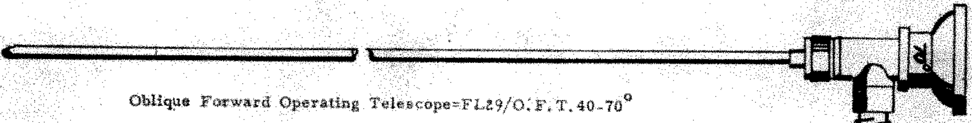
Stomahesive regular size will continue to be available.

SQUIBB

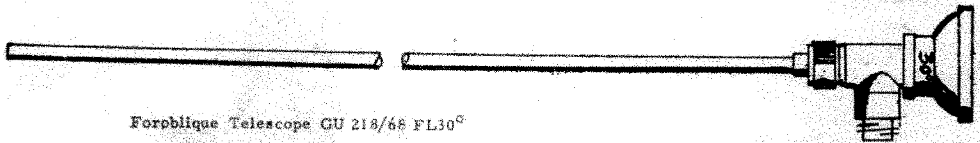
Full information available on request to: E. R. Squibb and Sons Limited, Regal House, Twickenham TW1 3QT.

G.U. – BLANDY CYSTO–RESECTOSCOPE

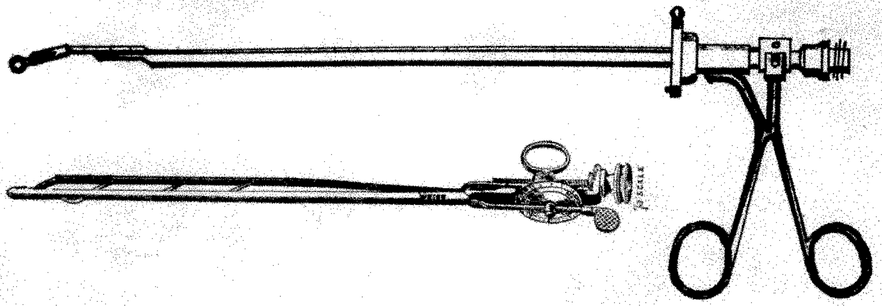




Oblique Forward Operating Telescope=FL29/O.F.T.40-70°



Foroblique Telescope GU 218/68 FL30°



Made by
THE GENITO-URINARY MANUFACTURING CO. LTD.
28a 33–34 Devonshire Street London W1N 2AJ
Telephone:
01–935 2835/6/7
Telegrams:
Cystoscope London W1

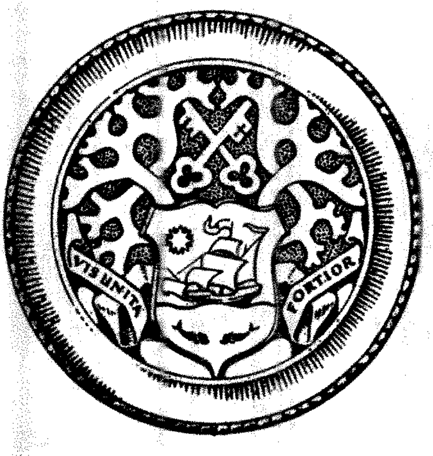
ISSN 0007-1331

15.11.76

BRITISH JOURNAL OF UROLOGY

Official Journal of the
British Association of Urological Surgeons

COLLEGE OF
LIBRARY



Volume 48 No 3

June 1976

E & S Livingstone

BRITISH JOURNAL OF UROLOGY

EDITOR
* W. KEITH YEATES

HON. TREASURER
* C. H. KINDER

ASSISTANT EDITORS
* G. D. CHISHOLM
* D. M. ESSENHIGH
* W. F. HENDRY
* W. SELBY TULLOCH

ASSISTANT EDITOR FOR AUSTRALASIA
G. F. MURNAGHAN

CONSULTING EDITORS
* DAVID BAND
* J. D. FERGUSSON

EDITORIAL COMMITTEE
Chairman D. INNES WILLIAMS*

G. H. BAINES, Birmingham
JOHN BALFOUR, Vancouver
D. R. BARNES, Cape Town
J. P. BLANDY, London
JEAN CHARBONNEAU, Montreal
C. A. C. CHARLTON, Bath
PHILIP CLARK, Leeds
B. N. COLABAWALLA, Bombay
M. H. DEVEREUX, Loughton, Essex
J. N. de KLERK, Cape Town
E. CHARLTON EDWARDS, Manchester
E. J. ENGLAND, Perth, W. Australia
H. FINE, Durban
ALBAN H. GEE, Sydney
N. O. K. GIBBON, Liverpool
JOHN GRIEVE, Dundee
A. R. HARRISON, London
D. K. KARANJAVALA, Bombay
J. A. KENNEDY, Belfast
W. K. KERR, Toronto
KENNETH J. MACKINNON, Montreal
J. W. F. MACKY, Auckland
JOHN P. MADDERN, Adelaide
J. P. MITCHELL, Bristol
*RICHARD A. MOGG, Cardiff
J. DERMOT O'FLYNN, Dublin
H. H. PEARSON, M.B.E., Canberra
J. S. PETERS, Melbourne
R. C. B. PUGH, London
P. J. M. RETIEF, Cape Town
CHARLES J. ROBSON, Toronto
L. STUART SCOTT, Glasgow
K. E. D. SHUTTLEWORTH, London
SARINDER MAN SINGH, Delhi
J. C. SMITH, Oxford
J. J. STEVENSON, London
J. H. STEYN, Aberdeen
W. BARR STIRLING, Glasgow
JOHN SWINNEY, M.C., Bunbury, W. Australia
G. C. TRESIDDER, London
P. J. P. VAN BLERK, Johannesburg
DAVID M. WALLACE, O.B.E., London
J. G. WATSON, Brisbane
R. H. WHITAKER, Cambridge
*J. L. WILLIAMS, Sheffield
J. F. R. WITHYCOMBE, Cambridge

* Members of Executive Committee

ST PETER'S MEDAL AWARDED TO

J. B. MACALPINE, 1949
R. OGIER WARD, 1951
TERENCE J. MILLIN, 1951
A. CLIFFORD MORSON, 1954
LESLIE N. PYRAH, 1959
CUTHBERT E. DUKES, 1960
DAVID BAND 1962
SIR ERIC RICHES, 1964

THE BRITISH ASSOCIATION OF UROLOGICAL SURGEONS

ARTHUR H. JACOBS, 1965
D. INNES WILLIAMS, 1967
H. HAMILTON STEWART, 1968
JOHN SWINNEY, 1969
SIR MICHAEL WOODRUFF, 1970
D. S. POOLE-WILSON, 1971
DAVID M. WALLACE, 1973
A. W. BADENOCH, 1974
HOWARD G. HANLEY, 1975

E. & S. Livingstone
Edinburgh and London
June 1976

Contents

UNIVERSITY COLLEGE OF MEDICINE LIBRARY

ORIGINAL ARTICLES

161 **Some Observations on the Medulla of the Kidney**
H. Fine and E. N. Keen

171 **Crossed Renal Ectopia with Colic: a Clinical Clue to Embryogenesis**
D. G. Romans, M. A. S. Jewett and C. J. Robson

175 **Hydronephrosis and Polycythaemia**
A. Sriman Narayana, F. Gallagher, D. G. Kelly and F. A. Duff

177 **A Simple Method for Studying the Formation of Calcium Oxalate**
D. June Sutor

183 **Circumcaval Ureter: A Report of Four Cases in Children with a Review of the Literature and a New Classification**
M. M. Kenawi and D. Innes Williams

193 **Abnormalities of Detrusor and Sphincter Function in Multiple Sclerosis**
Jens T. Andersen and William E. Bradley

199 **A Case of Behçet's Disease involving the Bladder**
G. F. Carswell

203 **Preliminary Communication: Cryosurgery for Prostatic Obstruction using Liquid Nitrous Oxide**
B. M. Wright

207 **Latent Carcinoma of the Prostate: the Probability of Identifying Small Lesions in Routine Histology**
G. S. Delides, G. Baltopoulos and N. X. Papaharalampous

211 **Introital Bacterial Flora—Effect of Increased Frequency of Micturition**
John M. Seddon, Andrew W. Bruce, Paul Chadwick and Donna Carter

SHORT CASE REPORTS

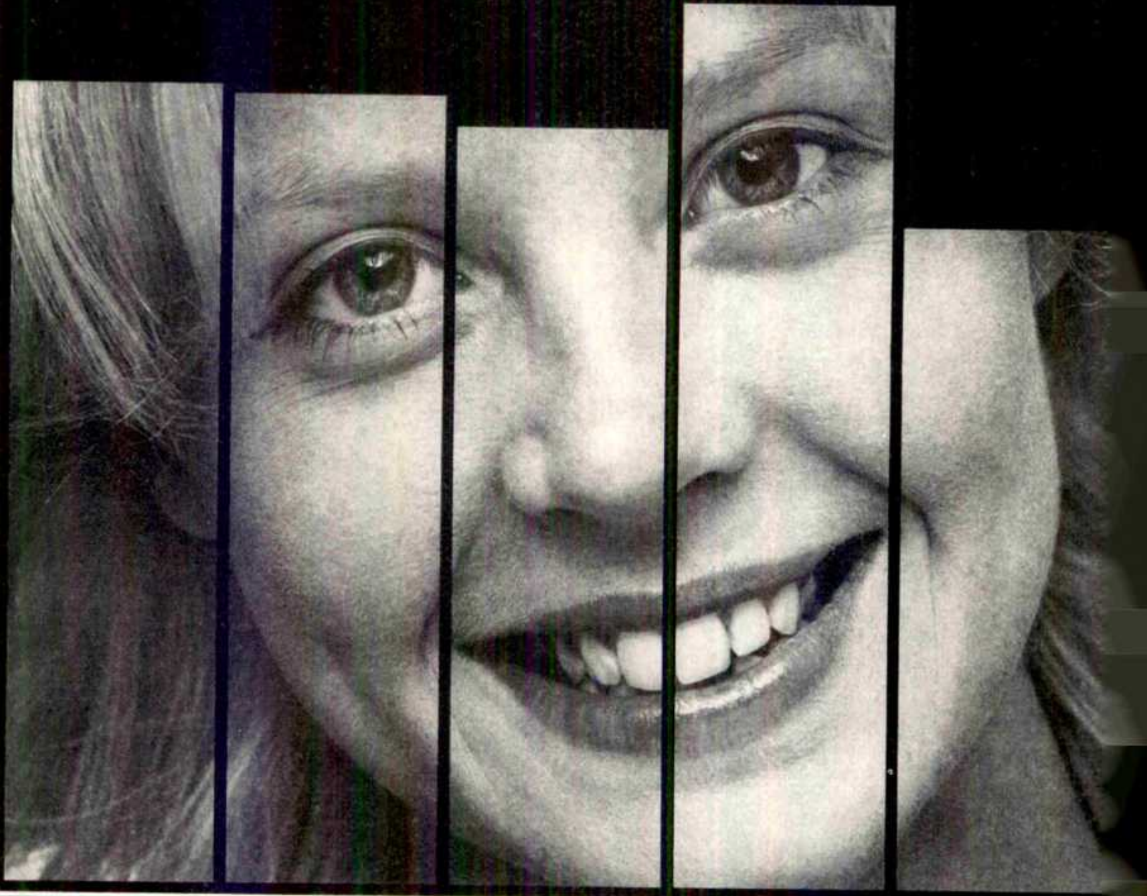
170 **Peritoneal Tuberculosis with Uretric Obstruction, Mimicking Retroperitoneal Fibrosis**
P. G. Bentley and D. R. Higgs

210 **Malignant Testicular Lymphoma in Brothers**
B. L. S. Gallagher and A. I. Hashmat

219 **Localised Primary Amyloidosis of the Bladder**
Richard A. Blath and James G. Bucy

ISSN 0007-1331

A 99.1% chance of success in U.T.I.

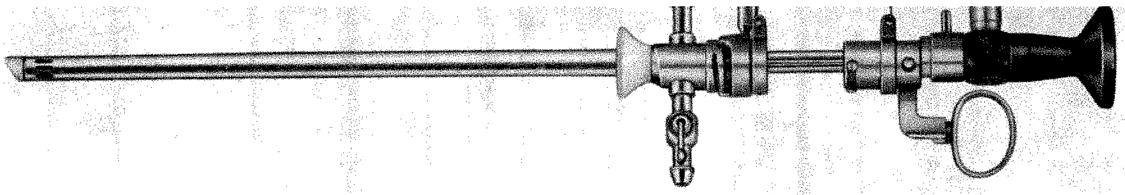


The chart above shows the percentage sensitivities of isolates from acute urinary infections against five commonly-used antibacterials. (From an *in-vitro* study involving 173 general practitioners). SEPTRIN was superior to all other oral antibacterials tested, with 99.1% of urinary pathogens sensitive.

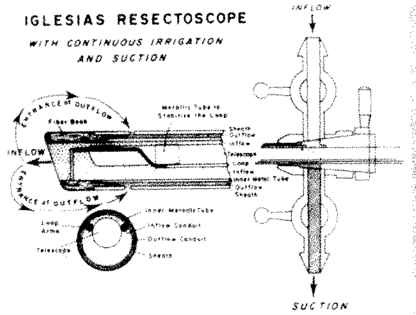
J int med Res (1974), 2, 40

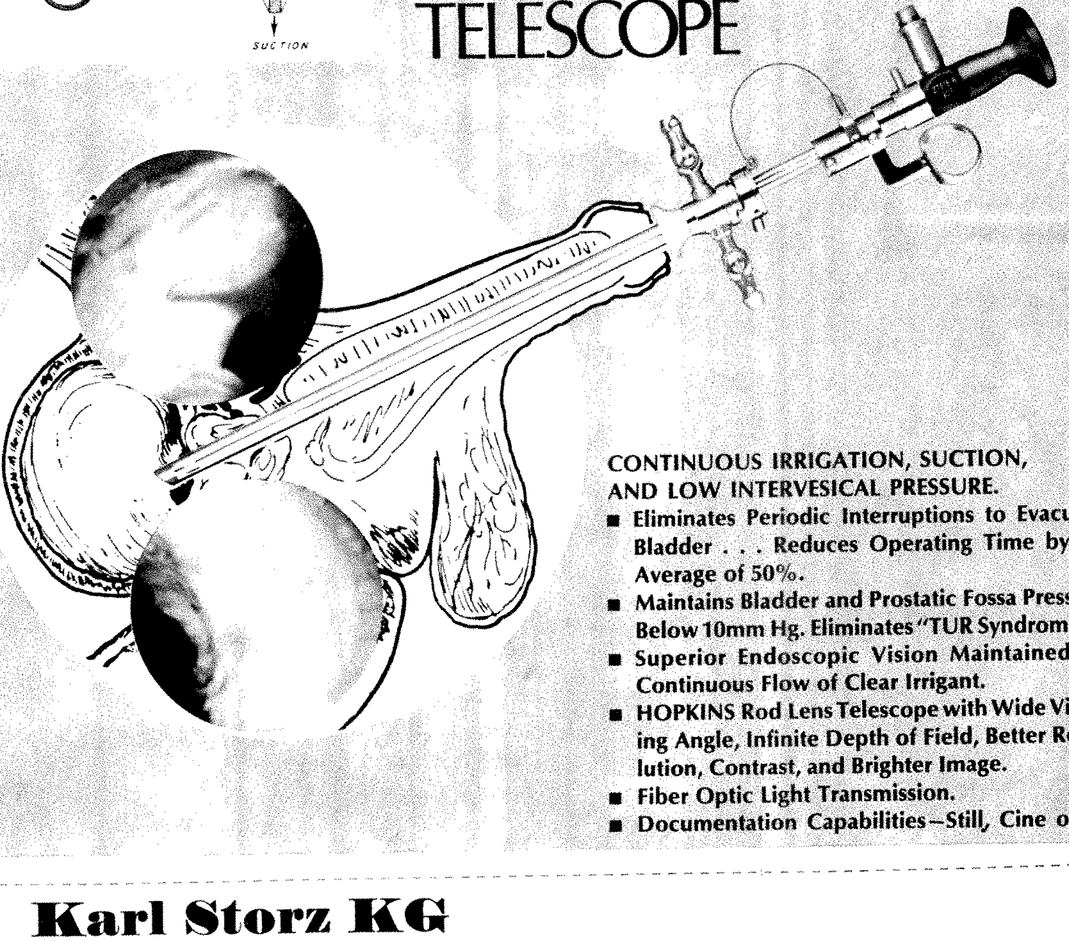
come
ontains
prim and
ethoxazole.
SCRIBING
TION IS AVAILABLE
EST.
e Medical Division
come Foundation Ltd
sted Herts

SEPTRIN first
TRADE MARK
in urinary tract infection



NEW IGLESIAS
CONTINUOUS IRRIGATION
RESECTOSCOPE
from Karl Storz
with
HOPKINS
TELESCOPE





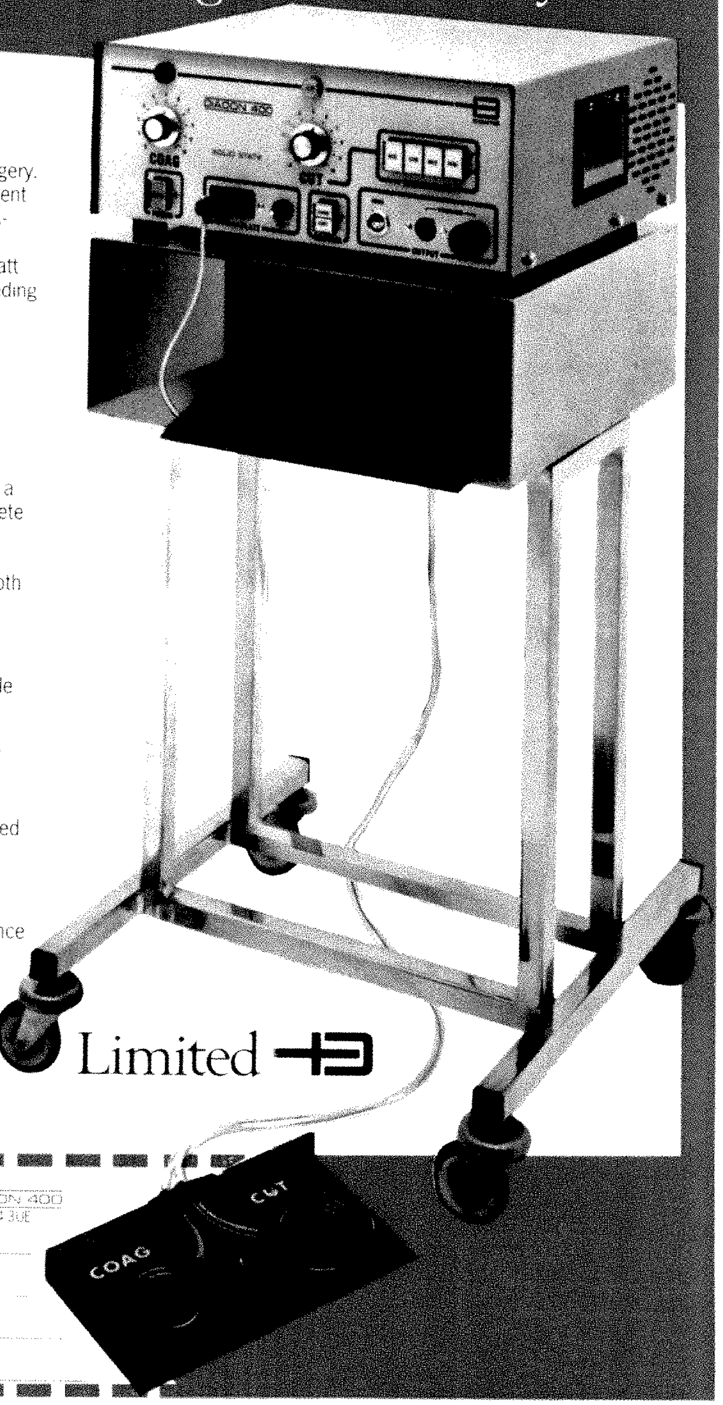
CONTINUOUS IRRIGATION, SUCTION,
AND LOW INTERVESICAL PRESSURE.

- Eliminates Periodic Interruptions to Evacuate Bladder . . . Reduces Operating Time by an Average of 50%.
- Maintains Bladder and Prostatic Fossa Pressure Below 10mm Hg. Eliminates "TUR Syndromes".
- Superior Endoscopic Vision Maintained by Continuous Flow of Clear Irrigant.
- HOPKINS Rod Lens Telescope with Wide Viewing Angle, Infinite Depth of Field, Better Resolution, Contrast, and Brighter Image.
- Fiber Optic Light Transmission.
- Documentation Capabilities—Still, Cine or TV.

Karl Storz KG
MANUFACTURER OF ENDOSCOPES
D-7200 TUTTLINGEN/W.-GERMANY - MITTELSTR. 8 - POSTFACH 400

UNITED KINGDOM AGENTS
RIMMER BROTHERS (RIMBROS LTD) - 18-19 AYLESBURY ST. - LONDON EC 1 R ODD
TEL. 01 253 7246

DIADON 400 Solid state surgical diathermy unit



Powerful output

Solid state generators in the DIADON 400 provide sufficient power for all types of surgery.
400 watts continuous cutting power, sufficient for even the most difficult underwater transurethral resection.
400 watt pulsed coagulation power (150 watt mean) sufficient to deal with all normal bleeding points encountered, even under water.
Individual output controls for cutting and coagulation allow smooth and accurate adjustment of output.

Pneumatic footswitch

To completely eliminate all electric current from the floor the DIADON 400 is fitted with a pneumatic footswitch. This provides complete safety where water and flammable gases are present.
The footswitch gives separate control for both the cutting and coagulation functions.

Optional hand control

The DIADON 400 provides facilities to enable the use of the DIADON hand control which eliminates the footswitch and gives the surgeon complete control of the cutting and coagulation functions at his fingertips.
The DIADON hand control takes the normal range of electrode tips and may be autoclaved or immersed in fluid.

Made to HTM8

The DIADON 400 is constructed in accordance with the Department of Health and Social Security safety recommendations HTM8.

Downs Surgical Limited

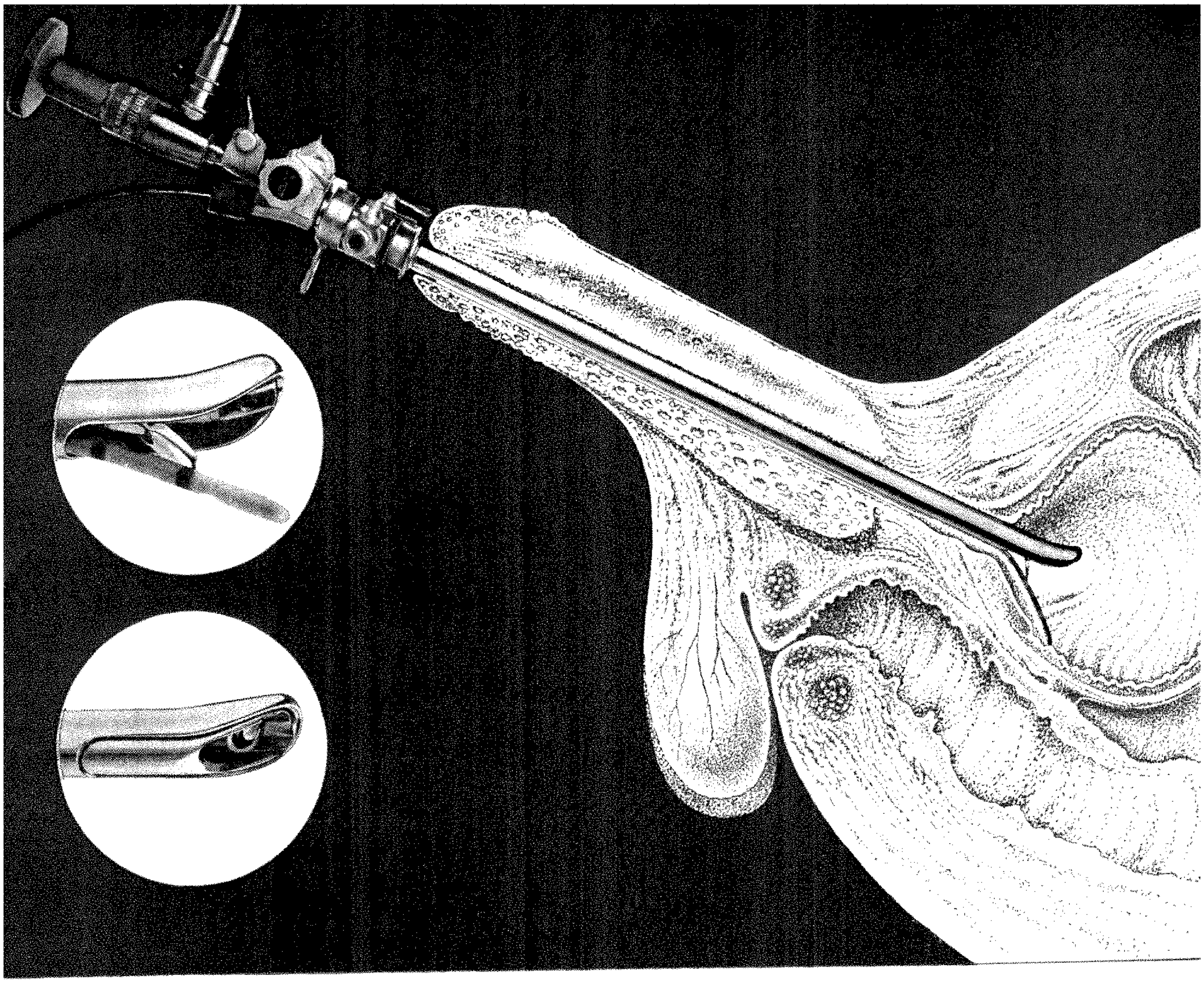
Complete coupon for an illustrated leaflet on the DIADON 400 and post to: Downs Surgical Limited, Mitcham, Surrey CR4 3UE

Name ……………………………………………

Address ……………………………………………

……………………………………………

……………………………………………



Introduce Microlens® to your patients

When you introduce the new ACM Microlens® System you simplify your urological procedures.

Cystoscopy, urethroscopy, resection and all general urological endoscopy can be accomplished with this remarkable system using only two telescopes and interchangeable components.

Microlens® is a new rod lens optical system with additional elements, which has been specifically developed for urological applications by American Cystoscope Makers Inc., the world's largest manufacturer of medical endoscopes.

Compared with previous telescopes Microlens® offers the surgeon a larger, sharper image which is crisp and clear right to the edges. It covers a broader field too, with much less distortion.

Superior optics, interchangeability and simplicity are just three of the many plus points of ACM urological instruments. Like all ACM products they are well-engineered, durable and exceptionally easy to use, as well as being easy on the eye. There's a full range of specialised instruments and accessories, including a teaching attachment and a paediatric system.

For full details of the new ACM Microlens® urological system (and for a demonstration, if you wish) please telephone or write to the address belo

ACM ENDOSCOPY LIMITED

Park House, 22 Park Street, Croydon, Surrey, CRO OYH. Telephone 01-686 4241.

ACM

ACM Endoscopes - still clearly the best for gastro-enterology, bronchoscopy, urology, gynaecology and teaching.

Instructions to Authors

The *British Journal of Urology* welcomes original contributions on urological subjects from all parts of the world. The papers are accepted for consideration on the understanding that their contents have not been published in whole or in part elsewhere and that they are subject to editorial revision.

Any paper may be sent initially to a member of the Editorial Committee for comment and advice on its being suitable to be considered for publication.

A leaflet showing the criteria used in the assessment of papers submitted for consideration is available from the Editor on request.

Authors should supply their qualifications, main appointment, and the name and address of the hospital or the laboratory.

Please indicate name and address to which requests for reprints should be made.

Format and content of papers

The text of articles submitted for publication should be typewritten in double-spacing on paper sheet size 22 × 32 cm (A4). There should be a minimum margin of 3 cm all round. The pages should be numbered.

Reports on clinical or laboratory investigation should as far as possible be organised into the following main sections: (1) Introduction, (2) Objective(s), (3) Patients or Materials, (4) Procedures or Methods, (5) Findings or Results, (6) Discussion and (7) Conclusions with (8) a Summary at the end.

Nephrology. Papers on disorders of renal function of interest to the urological surgeon are welcome.

Ethics. When relevant, authors must include a statement on the ethical aspects of their research.

Reports of clinical cases should consist of the following sections: (1) Introduction, (2) Case Reports and (3) Comment with (4) a Summary at the end.

Reports on single cases. Papers reporting a single case are considered for publication as full papers only when the case has definite instructional value. The Introduction and Discussion should not be disproportionate to the case presentation. *An abbreviated version suitable for publication as a Short Case Report as an alternative must also be submitted.*

In all full papers the literature should be summarised as concisely as is consistent with establishing the necessary basis for new material. Discussions and Conclusions should be strictly limited to the results presented. Recapitulation from previous sections should be avoided whenever possible. Summaries should be composed of very brief statements about each of the main sections.

Headings. The relative importance of sub-headings should be clearly indicated.

Numbers. All numbers should be shown as figures rather than as words.

References. *The accuracy of references is the responsibility of the author.* Only papers closely related to the author's work should be referred to; exhaustive lists should be avoided. *References in the text* should be quoted by the author's name(s) and year of publication. Unless there are more than 3 authors, all the names should be stated at the first reference; if there are more than 3 authors only the first author plus *et al.* is used. In subsequent references to the same paper, *et al.* is used if there are more than 2 authors. *The list of references at the end of the paper* should be in alphabetical order. *References to journals* should include the name(s) and initials of the author(s), year, title of paper, name of journal in full, volume number and the numbers of the first and last pages. *References to books* should include the name and initials of the author, year, title of book, number of edition, city of publication, name of publishing house, and page number(s).

Illustrations. Photographs and radiographs should be submitted in the form of *matt* prints of a size no larger than 17·5 × 12·5 cm and no smaller than 9 × 6·5 cm. All figures should be sent unmounted. The number of the figure, the name of the author and the "top" of the illustration should be indicated lightly in pencil on the back. The magnification of micro-photographs should be stated. Graphs and diagrams should be drawn in Indian ink. *Lettering and figures must be indicated only on a transparent cover.* Legends to figures should be typewritten on a separate sheet of the manuscript. Tables, unless they are very small, should also be typewritten on separate sheets. The position of illustrations and tables should be indicated in the margin of the text.

There is no charge to contributors for the printing of black-and-white illustrations on papers accepted for publication. Illustrations in colour may be accepted at the discretion of the Editor provided he is of the opinion that these are necessary for the improvement of the article. The author may be required to pay for the extra cost involved by the reproduction in colour.

Reprints

25 offprints are supplied to the first named author only, free. Forms for ordering offprints will be sent with the proofs for correction; the order form should be returned with the corrected proofs within 7 days.

Continued on page v

Travelling Fellowship

The British Association of Urological Surgeons offers a Travelling Fellowship of £250 based on the best paper published in the *British Journal of Urology* in the preceding year including those papers presented at the British Association of Urological Surgeons Annual Meeting.

Candidates for the prize must be Fellows of one of the Royal Colleges of Surgeons in the British Isles, Canada, Australasia or South Africa who are in the course of urological training or who have obtained consultant posts within 10 years of the date of submission of the paper.

The Fellowship will be awarded for the best paper published in the Journal from the April issue of one year to the February issue of the following year.

Authors of papers with multiple authorship should indicate which one of their number should be awarded the Fellowship in the event of their contribution being selected.

Three assessors will be appointed by the Council to make recommendations on the award of the Fellowship. The Council reserves the right not to make an award in any one year.

The award will be announced at the June meeting of the Association.

Short Case Reports

Brief reports (preferably with 1 and not more than 2 illustrations) of unusual cases not published elsewhere may be submitted as summaries of not more than 200 words for consideration for publication as Short Case Reports. They should comprise (1) a Title, (2) Case description and (3) a brief Comment. The authors and references are each limited to 3. The titles of these reports will usually be recorded in Index Medicus and by MEDLARS.

Preliminary Communications

Preliminary communications of original work may be submitted as short papers. The communication should be divided into 4 sections: (1) Objectives, (2) Materials and Methods, (3) Preliminary results, (4) Interpretation or Significance of Results.

Discussion of Papers

Questions or criticisms concerning recently published paper may be sent to the Editor, who will refer them to the authors. The readers' comments and authors' replies may subsequently be published together.

There is no other correspondence section in the Journal.

Suggested Projects for Urological Research

Clinicians who have ideas for research projects, but have no opportunity for carrying them out, may submit them for publication in the above section. The communication should not be longer than 500 words. References will be limited to 6.

Abstracts from Current Urological Literature

Urologists who are willing to undertake abstracting of urological articles appearing in other journals should communicate with the Assistant Editor, Mr. W. Selby Tulloch, at the Department of Urology, Western General Hospital, Edinburgh, EH4 2XU.

Addresses

With the exceptions noted below, all editorial communications, including books for review, should be addressed to the Editor, Mr. W. Keith Yeates, at the Department of Urology, Newcastle General Hospital, Newcastle upon Tyne, NE4 6BE.

Preliminary Communications on Research Projects and *Suggested Projects for Urological Research* should be submitted to the Assistant Editor, Mr G. D. Chisholm, at The Urology Unit, Hammersmith Hospital, Royal Postgraduate Medical School, London, W12 0HS.

Short Case Reports (presented as described above) should be sent to the Assistant Editor, Mr W. F. Hendry, Institute of Urology, University of London, 172 Shaftesbury Avenue, London, WC2H 8JE.

Communications concerning the Abstract Section should be sent to the Assistant Editor, Mr W. Selby Tulloch, at the Department of Urology, Western General Hospital, Edinburgh, EH4 2XU.

Publishing, Advertisement and other enquiries: E. & S. Livingstone, Longman Group Ltd., Journals Division, Longman House, Burnt Mill, Harlow, Essex CM20 2JE.

Subscriptions

The Journal is published in February, April, June, August, October and December. Subscription £17·00 (U.S.A. $45.00) per annum, post free. Single copies £3·00 (U.S.A. $9.00) each. Previous volumes and parts of volumes (if available) may be obtained from the publishers, price £6.00 per volume or 75p for single parts.

Subscription enquiries: Messrs E. & S. Livingstone, Journals Division, 43/45 Annandale Street, Edinburgh, EH7 4AT.

Subscriptions for U.S.A. should be sent to The Williams and Wilkins Company, 428 East Preston Street, Baltimore, Maryland, U.S.A.

All rights reserved. No part of this publication may be reproduced, stored in a retrieval system, or transmitted in any form or by any means, electronic, mechanical, photo-copying, recording or otherwise, without the prior permission of the copyright owner.

Nothing has changed except our name

Please note that we have changed our company title from Wappler Endoscopy to ACM Endoscopy Limited. We have taken this step to associate ourselves more firmly with our parent company American Cystoscope Makers Inc. (ACMI) and with the name by which our products are known internationally.

But only the name of our company has changed. Nothing else. The address remains the same. So does the telephone number. You will still speak to and deal with the same people.

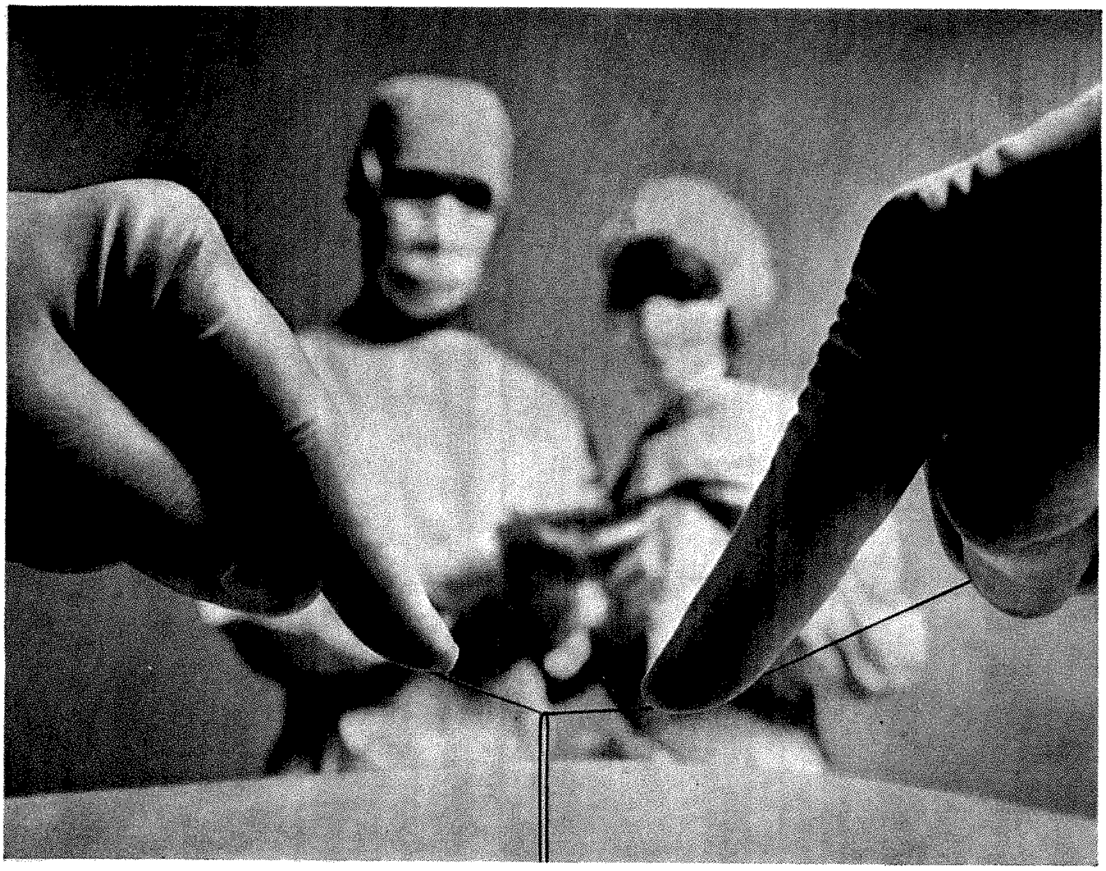
And, of course, ACM endoscopes are still clearly the best and the range is as comprehensive as ever.

ACM ENDOSCOPY LIMITED
Park House, 22 Park Street,
Croydon, Surrey, CR0 0YH. Telephone 01-686 4241.

ACM

ACM Endoscopes - still clearly the best
for gastro-enterology, bronchoscopy,
urology, gynaecology and teaching.

Monofilament Smooth



Because of the even diameter of ETHICON* Surgical Gut along its entire length, the smooth monofilament surface finish makes passage through tissue easier and smoother and produces less trauma.

Catgut beds down smoothly and securely with even the first throw of the knot and holds securely and strongly with standard surgical knots.

But we're not stopping there. Through research and development we continually strive to offer you, the surgeon, the finest absorbable suture available—but that's only some of the reasons why ETHICON surgical gut is today's most widely used suture material.

Catgut places a world of experience at your fingertips.

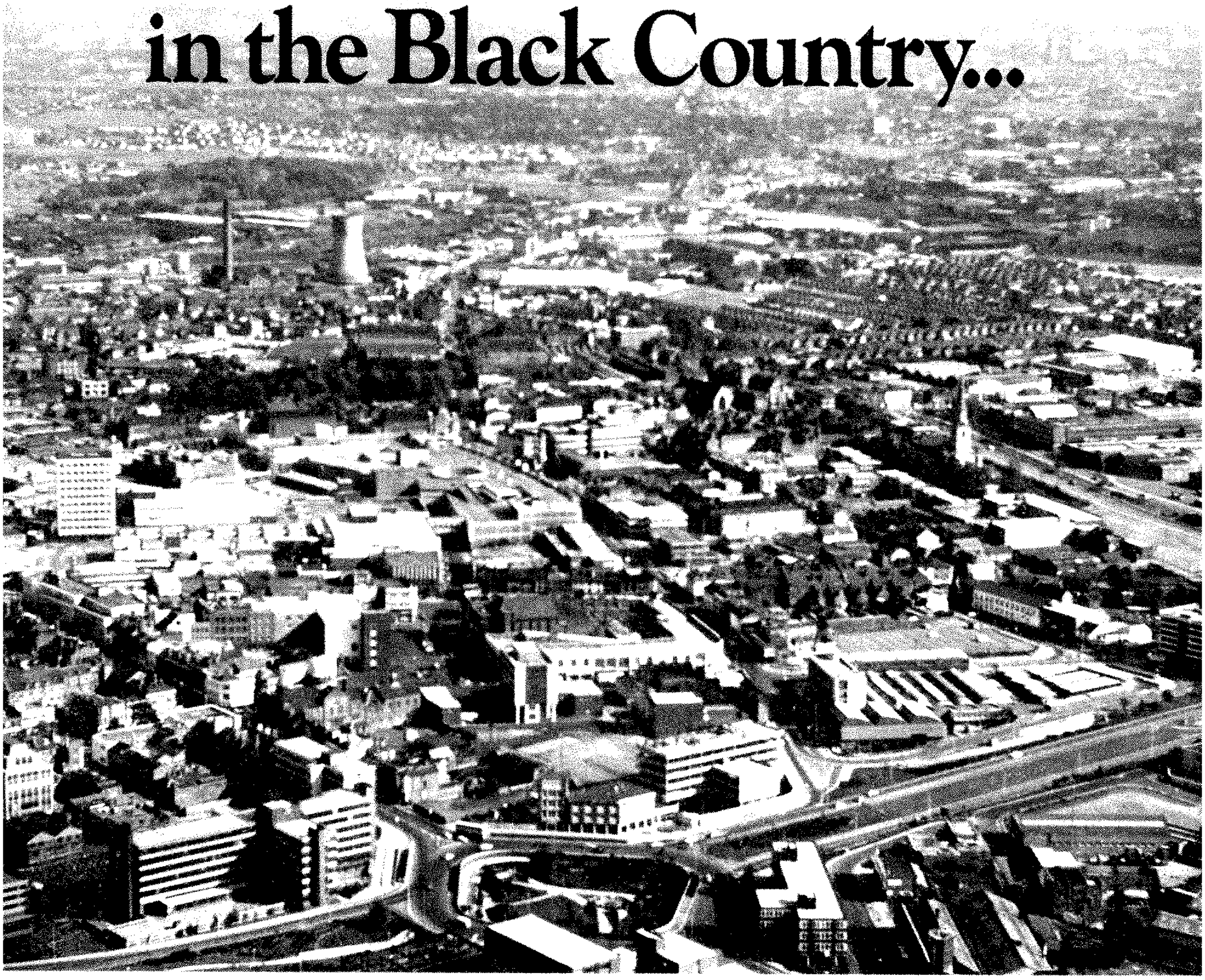
ETHICON

When the difference is between being sure and being absolutely certain.

PLR 0508/5002

© ETHICON Ltd 1976 *Trademark

Amoxil making all the difference in the Black Country...

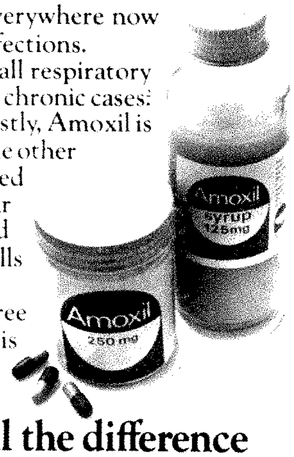


And throughout Britain. Because doctors everywhere now recognise the advantages of Amoxil in respiratory infections.

Amoxil ensures faster relief of symptoms[1] for all respiratory patients and longer periods free from infection for the chronic cases.[2]

Three main factors are responsible for this. Firstly, Amoxil is more completely absorbed into serum.[3] Secondly, unlike other antibiotics it penetrates equally well through inflamed and uninflamed bronchial membrane barriers[4] to clear even the most entrenched pockets of infection.[5] And thirdly, extensive studies have shown that Amoxil kills bacteria more rapidly than other antibiotics.[6,7]

These three factors, together with a trouble-free dosage, contribute to the Amoxil difference which is appreciated by doctors and patients everywhere.



makes all the difference
in respiratory infections everywhere.

ancet (1974), 212, 123.
therapy (1973), 18, (Suppl.) (19), 1.
l J., (1972), 3, 13.
a Med. LCS (1974) No. 326, 130.
d. J., (1973), 47, 719.
crob. Ag. Chem. (1975), 7, (2), 179.
otics under the Microscope'. A film
vailable to the medical profession.

ribing information on Amoxil (regd.),
tn, is available from Bencard,
st Road, Brentford, Middlesex.

encard

In Radiography

Conray Contrast Media

Products of distinction in their substance and shadow

'Conray' contrast media are formulations of either meglumine iothalamate, sodium iothalamate or combinations of the two. These high iodine/low viscosity preparations have an established record of excellence in providing wide margins of safety and tolerance for the patient together with optimum visualization in a comprehensive range of radiographic procedures.

Full information on 'Conray' 280, 'Conray' 325, 'Conray' 420, Cardio-'Conray', Retro-'Conray' and Gastro-'Conray' supplied on request to May & Baker Ltd Dagenham Essex RM10 7XS
*trade mark of Mallinckrodt Inc.

Conray*
Contrast Media–
A salt for all reasons
A view of all regions

M&B May & Baker

A member of the Rhône-Poulenc Group of Companies

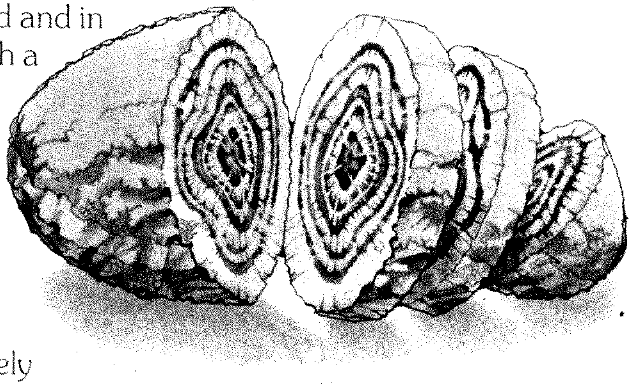
MA 3132

Diet and renal stones. The inside story.

Traditionally, patients with idiopathic hypercalciuria have been treated with a low calcium diet.

Indeed, "A diet with a very low calcium content, less than 50 mg daily, should provide an effective method of controlling calciuria."[1]

However, "due to the presence of calcium in so many kinds of food and in drinking water, such a diet is hardly possible. It is not palatable and would lack many indispensable trace elements."[1] Many foodstuffs contain a deceptively high level of calcium. A meal consisting of lamb stew can yield more calcium than the recommended allowance.[2]



This is why Whatman Sodium Cellulose Phosphate is being used increasingly as adjunctive treatment for idiopathic hypercalciuria. Whatman Sodium Cellulose Phosphate reduces calcium absorption and prevents renal stone formation.[3]

1. *Brit J Urol*, (1973), **45**, 136.
2. *Composition of Foods*, (1960), MRC Report 297, HMSO, London.
3. *American J Med*, (1971), **50**, 67.

Whatman®

Sodium Cellulose Phosphate

Fundamental treatment for idiopathic hypercalciuria.

Further information and data sheet on request from Whatman Biochemicals Limited,
Springfield Mill, Maidstone, Kent ME14 2LE. Telephone, Maidstone 673841. Telex: 96113.

® Registered trade mark of Whatman Limited

0651

British Journal of Urology (1976), **48**, 161-169 ©

Some Observations on the Medulla of the Kidney

H. FINE and E. N. KEEN

Department of Anatomy, University of Natal, Durban

With improvements in surgical and radiological manipulations of the kidney it has become necessary to know more about the anatomy of the kidney.

In the latter half of the last century and early this century anatomists like Testut (1895) and Symington (1914) had already described some of what is now being restated. Unfortunately these descriptions have largely been omitted from modern textbooks (Cunningham, 1937; Gray, 1973). Hodson (1972) has gone a long way to remedy this situation, in his lucid description of the lobar arrangement. The terminology which he suggests is used here.

Terminology

Hodson has named the various parts of the cortex as follows: *Cortical Septa* are the portions of cortex between adjoining medullary pyramids and which extend from the peripheral *mantle* of cortex (v.i.) inwards into the renal sinus. They are formed by fusion of the layers of cortex draining into the related pyramids. He recognised *Transverse* septa which extend across the front and back of the kidney (Figs. 1 and 2) and a *Longitudinal* septum which runs vertically down the parenchyma lateral to the sinus, separating anterior from posterior renal pyramids in the region between the two ends of the kidney. The *Centrilobar* cortex covers the base of its pyramid and conceals it from the surface of the kidney. The centrilobar cortex of a lobe is continuous with that of its neighbours and collectively the centrilobar cortex of all the lobes forms a *Mantle* of cortex which one sees on the surface of the kidneys (Figs. 1 and 2). The medullary mass of each renal lobe is the *Pyramid*. The latter is thus covered on its "sides" by the surrounding septa and over its "base" by its centrilobar cortex.

Materials and Methods

50 kidneys have been studied.

In 27 the pelvi-calyceal systems were filled with dye and X-rayed. They were then dissected, using a dissecting microscope, through the sinus down to the attachments of the calyces, exposing the papillae fully by removing the calyces almost at their attachments. The remainder of the parenchyma of these kidneys was sectioned in various planes, vertical, oblique and at right angles to the long axis and 5 of these were also sectioned transversely. In 10 serial longitudinal sections at right angles to the "flat" were made of the whole kidney. In 4 more latex was injected into the arteries and in 2 resin, before dissection. In 1 latex-injected and 5 others the cortex was teased off the medulla to expose the latter. 2 were bivalved and the walls of the sinuses were dissected and displayed.

In addition a number of resin casts of vessels in acid digested kidneys were studied. 2 kidneys were randomly dissected and studied.

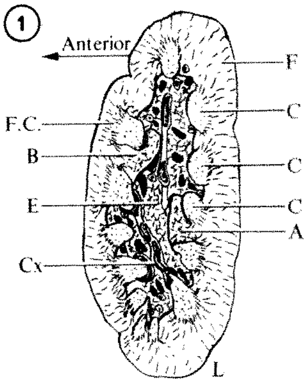
The kidneys were necropsy specimens from Indian and African subjects and ranged in age from stillborn through to adults. A number of foetal kidneys were also studied by microscopic dissection to see the cortical arrangement.

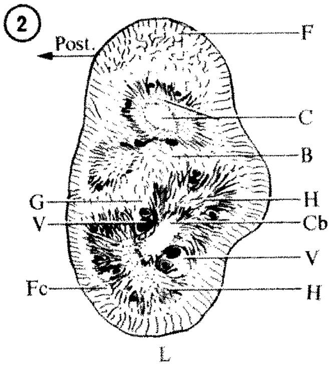
Findings

We were able to confirm substantially Hodson's descriptions with 1 exception. We found that in most kidneys the hilus tended to lie posteriorly rather than anteriorly as claimed by him. In order to facilitate description some additional terminology is suggested.

We have found it necessary to subdivide the septa into the following types:

1. *Major* septa are those septa described by Hodson. In addition, however, we have observed that some major septa entirely or in part do not extend as far as the sinus proper but only reach extensions from the sinus (interlobar





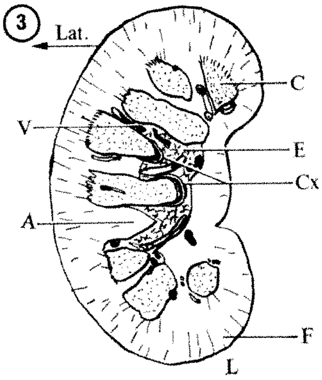


Fig. 1. Diagram from photograph of right kidney. Longitudinal section across the flat near the centre plane.
Fig. 2. Diagram from photograph of kidney. Superficial longitudinal section in the flat so that the ends are excluded.
Fig. 3. Diagram from photograph of kidney. Longitudinal section in the flat through the sinus close to the posterior wall of the sinus. The medullary masses lie across the kidney and are elongated. The posterior intermediate septum A bulges into the sinus.

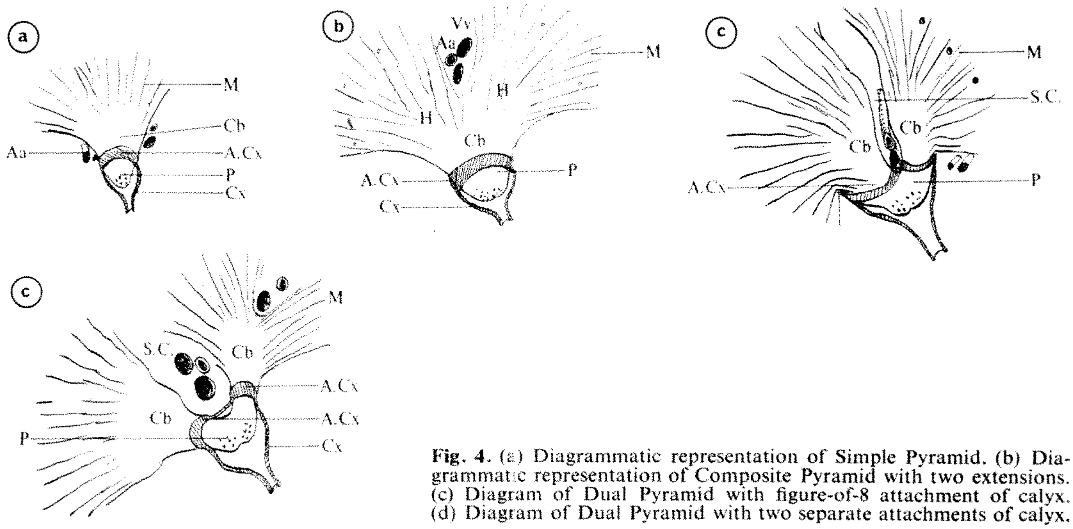
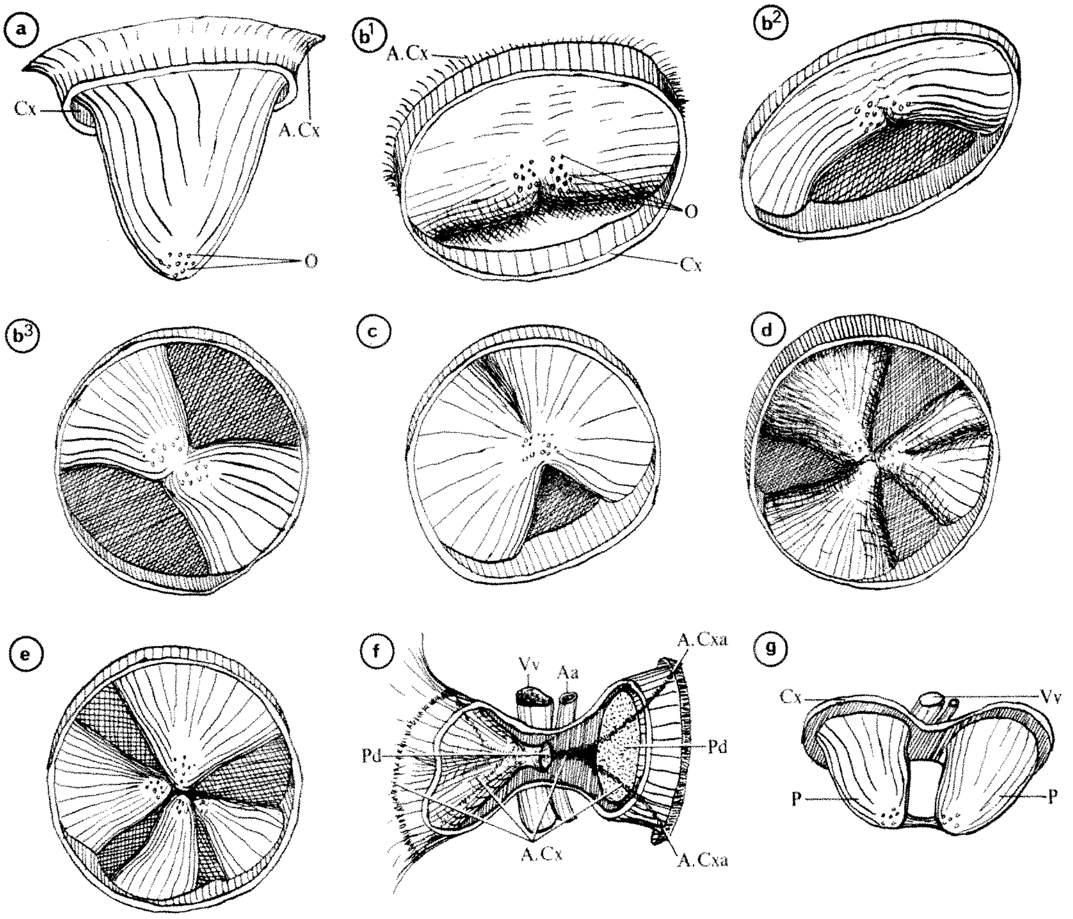


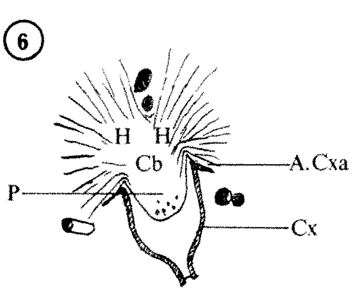
Fig. 4. (a) Diagrammatic representation of Simple Pyramid. (b) Diagrammatic representation of Composite Pyramid with two extensions. (c) Diagram of Dual Pyramid with figure-of-8 attachment of calyx. (d) Diagram of Dual Pyramid with two separate attachments of calyx.

Key:

A.	Posterior intermediate major septum. In Figure 1 it bulges far into the sinus and overlaps a body of a pyramid C.
A.Cx.	Calyceal Collar.
Aa.	Arcuate Artery.
A.Cxa	Calyceal collar forming acute angle with wall of calyx.
B.	Major Septum. In Figure 1 it is the Anterior Intermediate Septum overlapping the body of a pyramid.
C	Pyramids.
Cc.	Composite Pyramid.
Cb.	Body of Pyramid.
Cx.	Calyx. Cut edge of calyx in Figure 7.
D.	Vascular grooves between canal orifices. See Figure 7.
E.	Fibro-fatty tissues in the sinus.
F.	Cortex.
Fc.	Centrilobar Cortex in Mantle
G.	Minor Septum.
H.	Medullary Extension.
L.	Lower end of Kidney
M.	Medullary Rays.
O.	Duct Orifices
P.	Papilla (with Duct orifices).
Pd.	Papilla with segment removed to show calyceal attachment on deep aspect of papilla, in a figure-of-8 attachment. See Figure 5f.
S.C.	Interpyramidal Cleft which is extension of sinus containing arcuate vessels.
Vv.	Veins.
V.	Vascular canal.



Figs. 5. a-g, Diagrams of dissections: Shapes of papillae with calyces cut off close to their attachments to show the papillae. (a) Simple papilla, (b1) Straight-ridged papilla. (b2) Crescentic-ridged papilla. (b3) Bifid papilla, (c) Tent-like papilla, (d) Trifid papilla (e) Cruciate papilla (f) Bifid papilla from Dual Pyramid showing figure-of-8 attachment of calyx. (g) Two papillae linked by a band.



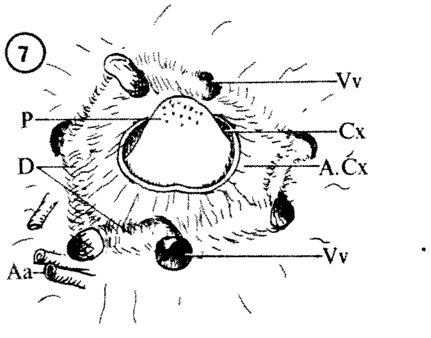


Fig. 6. Calyx with acutely angled collar.

Fig. 7. Diagram of photograph. Papilla with surrounding vascular grooves and canal orifices.

clefts) which separate the *Bodies* (v.i.) of the adjacent pyramids (Figs. 1 and 2). These clefts contain vessels and connective tissue (see vascular canals).

2. *Minor* septa (Figs. 1 and 2) differ from major septa in that they do not separate 1 pyramid from another but project into clefts between adjoining extensions of the pyramid. They project from the major septa or from the centrilobar cortex, and extend as far as the body of the pyramid without reaching the sinus. They contain tubules which empty only into the pyramid to which they are related and not into 2 adjoining pyramids.

3. Certain major cortical septa are sufficiently prominent and constantly present to warrant giving them specific names.
   (*a*) Between the renal lobes which drain into the upper and lower groups of calyces respectively (*i.e.* the upper group and lower group lobes) there are frequently large transverse septa. These we call the *Intermediate* septa. In more than 50% of kidneys there are both anterior and posterior intermediate septa, the anterior usually being situated at a higher level than the posterior (Fig. 1). They fuse laterally or, when it is present, meet the longitudinal septum. In the minority of kidneys in which there is a middle group of pyramids (draining into a middle group of calyces) there is a smaller additional transverse septum between the middle and lower groups of pyramids. The septum between the middle and upper groups of pyramids is still usually noticeably large and deserves to retain the name anterior intermediate septum. The posterior intermediate septum separates the medulla draining into the upper calyces from the lower pyramids (draining into the lower calyces) at the back of the kidney.
   (*b*) Occasionally there are major septa at the ends of the kidney. In such kidneys there will be 2 or more end lobes but most kidneys have a single large and composite lobe at each end. In the region intermediate between the ends there are usually additional major septa in front and behind and correspondingly more lobes.
   (*c*) In about a 4th of the kidneys there is a large longitudinal septum laterally and another posteriorly of various lengths in different kidneys, separating 3 rows of pyramids (see also "Central Pyramids"). In the remaining three-fourths of the kidneys there is a single large longitudinal septum laterally. It extends the full length of the central portion (between the end pyramids) of the kidney in a minority of these and for a shorter distance in the remainder.

Medulla

There were multiple lobes at the ends, in about a 4th of the kidneys that could be studied for this feature (37 specimens) and single composite end lobes in the remainder. Between the end pyramids there were from 1 to 3 major transverse septa anteriorly and similar numbers posteriorly, separating transversely lying pyramids (Figs. 2 and 3).

The medullary masses are in fact not truly pyramidal in shape but for historical reasons the term pyramid is used to denote the medullary tissue of a single lobe. Many pyramids have two or more *Extensions* on their sides and these are darker than the rest of the pyramid. Between the extensions are clefts in which are wedge-shaped cortical projections whose apices are related to arcuate vessels. These cortical projections are the *Minor* septa (Fig. 2). The medullary rays enter the extensions of the pyramid from the related surrounding cortex of that lobe. The extensions are short and converge on the paler central portion of the pyramid which can usefully be named the *Body* of the pyramid (Figs. 2 and 4a to d). The papilla projects from the body into the sinus where it is surrounded by its calyx.

In summary a renal lobe as here described consists of a single pyramid surrounded by the cortex which drains into it and empties itself through its papilla.

Types of Pyramids (Figs. 2 and 4a to d)

1. A pyramid with a single extension and a round conical papilla is a *simple* pyramid.
2. A pyramid with more than 1 extension and of irregular shape is regarded as *composite* (Testut, 1895). The various extensions of a composite pyramid may be more or less separated with correspondingly large or small septa intervening. In a few instances the separation is complete except for the papilla and such an arrangement is regarded as a *dual* pyramid belonging to a single lobe. In no instance was there 1 pyramid with multiple separate papillae. A composite pyramid may drain cortex on both the front and the back of a kidney, whereas a simple one usually drains only one aspect.

Arrangement of Pyramids (Figs. 1 and 3)

The kidney has a duality of structure and development which is evident in the 2 major groups of calyces, *viz.* the upper group and the lower group. The lobes which drain into these groups may likewise be categorised as upper and lower groups of lobes. The middle calyces belong developmentally with the lower group and so do the lobes. They will therefore be included with these as far as is possible (Fine and Keen, 1966).

Table

	Total numbers of papillae	Average Nos.
Papillae in 23 kidneys	218	9
Lower	130	5
Upper	88	4
Anterior	141	6
Posterior	77	3
Simple	105	4
Composite	113	5
Composite Anterior	73	3
Composite Posterior	40	2

The area of the kidney which extends from the level of the upper border of the sinus to the level of its lower border is regarded as the *Central* region of the kidney, and the lobes herein as the central lobes. The lobes occupying the ends of the kidneys have been called the *End* lobes to distinguish them from those in the central region.

Where a papilla was situated on the anterior or posterior wall of the sinus we regarded the pyramid as being anterior or posterior respectively, even when it drained some cortex on the opposite side. The pyramids of the central region of the kidney were often elongated masses of medulla lying transversely across the kidney (Fig. 3), both in front and behind the sinus, and sometimes broken up into 2 or 3 pyramids by short longitudinal major septa. Sometimes a short or longer longitudinal septum served to separate the anterior from the posterior pyramids. Such septa were not universally present, however, and the distinction was then more difficult. As with the calyces, the upper group of lobes includes the upper end lobes and the posterior lobes of the central region as far down as the posterior intermediate septum, while the lower group includes the lower end lobes and the anterior lobes of the central region up to the anterior intermediate septum (Fig. 1) (Fine and Keen, 1966).

The Central Pyramids. Number from 1 to 4 on either side of the sinus. These are not necessarily the same number in the front and back of the same kidney. There are usually more in front than at the back (Table). Sometimes a large composite pyramid is present, when the transverse arrangement is not as obvious and the pyramids are fewer in number. In most kidneys there are a few pyramids in front and behind which are clearly seen to be anterior and posterior respectively. Their papillae are a few millimetres from the lateral margin of the sinus. The majority, however, lie more laterally between the former and their papillae are more difficult to place as anterior or posterior. As a result of this arrangement some authors have described 3 rows of papillae and pyramids (Testut, 1895). Longitudinal septa separate 3 rows of pyramids more frequently in the upper half of the kidney than the lower. In most specimens it is possible, using the dissecting microscope, to allocate an anterior or posterior position to most papillae and their pyramids.

The End Pyramids (Löfgren, 1949). Are usually composite and have a general contour which roughly conforms with that of the kidney. They drain cortex on the front and the back of the kidney. In a few kidneys, however (usually in the upper half of the kidney), there are 2 or more pyramids draining front and back separately. In such instances there are longitudinal septa extending into the ends of the kidneys from the central region. In some kidneys adjacent pyramids are separated from each other near the sinus by a deep cleft containing blood vessels and connective tissue. Beyond the cleft is a septum which is a short major one containing elements of the cortex of both renal lobes (Fig. 3).

The Papillae

Morphology

There is considerable variation in size and shape of the papillae of the same kidney (Fig. 5a to g). Depending on the position and number of extensions projecting from the body of the medullary pyramid there are corresponding ridges diverging from the apex of the papillae towards their respective extensions. In a few instances a separate pyramid contributes a ridge to a papilla so that a single papilla serves a dual pyramid (Figs. 4d and 5f). Separating the bodies of the dual pyramid are large blood vessels within a cleft extending from the sinus. The ridges consist of collecting tubules and small papillary vessels. Rarely 2 papillae are linked by a thin band or a narrow fold of mucous membrane (Fig. 5g). In the vast majority the line of continuity of papillary ridges is evident as a shallow groove, dimple or cleft and the duct openings are situated 1 or 2 mm away from the line of continuity.

The position of the ridges described above produces papillae of the following shapes (Fig. 5):

1. Conical (Fig. 5a).
2. Elongated, straight or V-shaped ridges, *i.e.* Bifid (Fig. 5b1 and 5b2).
3. Trifid or trifoliate, shaped like an arrowhead or triradiate (Fig. 5d).
4. Cruciate with four ridges (Figs. 5e to 8a).

LIBRARY OF MEDICINE

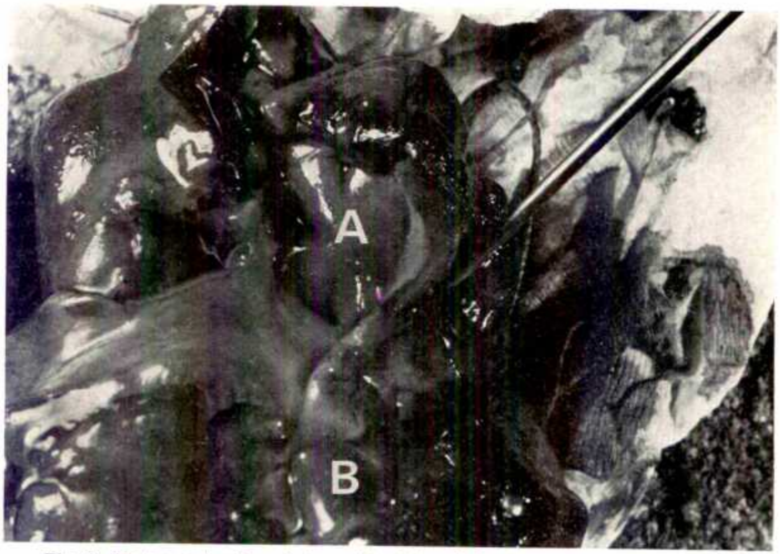


Fig. 8. Photograph of cruciate papilla (A) and simple conical papilla (B).

The conical type is a simple papilla and the remaining 3 types are composite papillae. The papillae at the ends of kidneys are usually composite. Occasionally they are unusually long, forming slender deep crescents with a groove at the middle (Fig. 5b2). In 23 of the 27 kidneys in which these were dissected, all the papillae were clearly defined. The types and distribution are shown in Table I. There are more papillae in the lower than the upper groups, which is in keeping with a previous study (Fine and Keen, 1966). The composite papillae exceed the simple in number, and there are more anterior than posterior papillae. In this series there are on average more papillae per kidney than in other reports (Cunningham, 1937; Emmett, 1964; Gray, 1973) *viz.* 9 compared with 7. This is perhaps due to a more careful search using radiography as well as the dissecting microscope.

Relation of Papillae to Calyces and their Attachments

Attachments of Calyces

Generally a calyx is attached to that surface of the body of the pyramid which faces the renal sinus and which it drains, by a broad *collar*. The periphery of the collar is attached to the following structures as they lie in proximity (Fig. 7):

1. Capsule of sinus over neighbouring cortex.
2. Lining of orifices of vascular canals.
3. Lining of vascular grooves between vascular canal orifices.

The collar usually forms an obtuse angle with the wall of the minor calyx but in many instances, especially at the ends of the kidneys, there is an *acute* angulation outward at the apex of the fornix of the calyx. This is so because in these instances the extensions of the pyramids form an acute angle with the body of the pyramid, where the collar is attached and the collar extends on to the extension forming a corresponding acute angle (Figs. 5f and 6).

In most instances a calyx surrounds only 1 papilla and has a single attachment encircling a discrete papilla. However, in a minority of instances, in composite papillae with dual pyramids, the attachment is complicated (Figs. 4c, 4d and 5f). There are two variations:

1. The calyx has 2 attachments, each surrounding ridges from the separated pyramids. Usually, in these the smaller pyramid has a single ridge and the larger has 2 or more ridges.
2. There is a single figure-of-8 attachment surrounding the separate ridges of the papilla to the dual pyramid, with the narrow segment of the 8 on the deep aspect of the papilla and separating the latter from the underlying blood vessels which are always present in such cases (Figs. 4c and 5f).

Occasionally too, where a pair of papillae are linked by a band or fold of mucous membrane (Fig. 5g) their minor calyces are fused and the wall of the calyces deep to the band or fold simply stretches across between the attachments, or may even form a shallow ridge separating the papillae (Figs. 4d and 5g). The calyx in such an instance is narrowed in the middle between the two papillae.

The variations described reflect degrees of separation of calyces, papillae and pyramids. In the majority of lobes separation is clear-cut but the arrangements described above are halts along the developmental road to complete separation (Potter, 1972).

Blood Vessels in the Sinus and Parenchyma

The Vascular Canals

Deep in the clefts between the extensions of the pyramids, and covered by minor septa, are connective-tissue-lined canals which contain arcuate arteries and veins and nerves and lymphatics (Figs. 2, 4b and d). These canals intercommunicate freely around their particular pyramid, as well as with those of adjacent pyramids. They form a network around the pyramid with its extensions passing through the interstices of the network.

The lining of the canals is continuous with that of the sinus. The arcuate veins are large and thin-walled, almost filling the canals, and are attached to the lining so that they cannot readily collapse. The rest of the contents occupy less space in the canals than the veins. The orifices of the vascular canals are in the sinus and are either wide and funnel-shaped, or consist of deep clefts between the bodies of the pyramids and the attachments of the calyces (Fig. 3). The orifices are linked by grooves surrounding the papillae. The grooves contain arteries or veins so that a vascular ring surrounds each calyx and papilla (Fig. 7).

The papillary zone is a slightly curved band at the lateral margin of the sinus, and is the area where most of the papillae are clustered. The long axis of the zone more or less bisects the kidney vertically across the "flat". Most of the interlobar vessels enter the parenchyma in the papillary zone around the papillae. A few enter at more remote points. The reason for this is that the papillary zone is the area where the cortex and medulla meet on the sinusoidal surface of the kidney. It is at this meeting point that the vessels enter the vascular canals which lie in the plane between the cortex and medulla.

Discussion

Development. The interpretation of the developmental status of the composite papillae and pyramids here described has been the subject of controversy, Emmett (1964), for example, holds that composite pyramids may have several papillae. This would imply that during development of the collecting system by binary division of the ampullae of the primitive ureter there is an area where more peripheral structures—*viz.* pyramids—are fused whilst more proximal structures *viz.*—papillae—remain discreet. We believe, on the contrary, that the composite structures here described are more rationally explained on a basis of uncompleted separation. In no instance in our view, do the structural details suggest fusion. We have not encountered composite pyramids with multiple papillae. If development is by binary division then logically one would expect more distal structures to show greater multiplicity than more proximal ones and not the reverse as Emmett implies.

It is reasonable therefore to regard all papillae, whether composite or simple together with the tubular systems which drain into them as parts of single lobes. It is hoped that this concept will eliminate the confusion encountered in the definition of a single renal lobe and papilla.

Architecture. We have not attempted to relate the general pattern of lobar arrangement to that described by Löfgren (1949). The rigid developmental pattern proposed by this author can only with difficulty be regarded as the unvarying developmental basis of the very varied patterns of lobes which are found in practice. On the other hand, a reasonably constant pattern of arrangement of medullary lobes can be stated for most kidneys. This consists of the end lobes and anterior and posterior central lobes. The pattern is not to be relied on in unusual cases, such as rotated, ectopic or fused kidneys.

Clinical Application. Hitherto descriptions of pathology in the kidney have been anatomically vague due to lack of definition of regions of the kidney and imprecise description of the parts of the lobes. More precision in observation in the operating theatre, the X-ray department and the mortuary will lead to a better understanding both of pathogenesis and surgical treatment of diseases of the kidney.

The radiological analysis of the structural patterns described leads to a clearer recognition of true abnormalities. An example is the localised shrinkage of cortex supplied by 1 or more arcuate arteries as described by Hodson (1972).

In surgery of the kidney, both in nephrostomy and nephrotomy, incision is most safely made through centrilobar cortex where the smaller arcuate vessels and their branches are the only vessels encountered. In nephrotomy bleeding from these is easily controlled by shallow mattress sutures.

Although lobar resection is not yet a standardised procedure, the basis for such an operation will be the anatomy outlined here. This is expected to apply especially in "bench-top" surgery.

In order to advance techniques in bench-top surgery it would seem to be necessary to avoid vessel damage and to be assured of haemostasis before returning the kidney to the patient. A logical method of lobar resection would be to use the avascular planes in the middle of major septa, and to ligate the arcuate vessels where they enter the vascular canals. This method would ensure a minimum of damaged and compromised tissue.

Some of the various forms of extravasation of dye in radiology of the kidney are more easily understood in the light of the anatomy here described:

1. Pyelo-interstitial backflow occurs between the tubules from a break in the mucous membrane on the papilla. This is more liable to occur in an unsupported corner of the mucosa, *e.g.* at the fornix or at the apex of the crevices of composite papillae.

2. Pyelovenous backflow occurs from the fornix of the calyx and is directed by the calyceal collar to the vascular canals where it tracks outside the vessels and lining of the canal, or it may break through the lining of a canal where this lies close to a weakness in the fornix (and this would be precisely opposite the orifice of a canal) and track within the canal. We agree with Sutton (1971) that it is in fact not intravenous backflow of dye.

3. Pyelo-sinus backflow follows the calyceal collar to the vascular canals and then turns towards the sinus rather than deeply along the vascular canals. This also is the result of a break in the lining of the canal.

Papillae and Calyces. Radiologically it is possible to recognise the type and position of a papilla, and to relate it to the pelvi-calyceal system as well as to decide whether it is anterior or posterior. From the shape of the papilla the morphology of the pyramid can be more or less accurately deduced. More detailed radiology will be described elsewhere. Pathology of the parenchyma can thus be located in relation to the papilla and calyx which drain the affected portion.

Dilated calyces in hydronephrosis compress the surrounding vascular collar and network, affecting the veins first. Later they flatten the papillae, further compress the vessels, and produce oedema followed by atrophy of the structures whose vessels are compressed. As the dilation progresses the calyces may bulge through the interstices of the vascular networks that surround them forming pockets, so that on X-ray it looks as if there are more calyces than there really are.

Many small recesses of the papillae are radiologically visible, and should not be mistaken for pathological cavities. The typical appearances of the end calyces on X-ray are largely due to the type of composite papillae within them and should not be confused with multiple calyces, or imagined as large calyces with multiple papillae within them. Likewise in the case of centrally situated calyces, the type of papilla will to a large extent determine the radiological appearance of that calyx.

It is useful to be familiar with the appearance of the various types of papillae when using the nephroscope or ureteroscope.

Summary

Terminology of the cortex of the kidney is discussed and some new terms are suggested.

Observations are described on 50 kidneys which have been injected and variously dissected. These include descriptions of the medulla, papillae and calyces.

Some developmental, radiological and surgical aspects are mentioned and suggestions for further study are made.

References

Cunningham, D. J. (1937). *Textbook of Anatomy*, 7th ed., London: Oxford University Press, pp. 694 *et seq.*

Emmett, J. L. (1964). *Clinical Urography*, 2nd ed., vol. 1, Philadelphia: Saunders, pp. 219 *et seq.*

Fine, H. and Keen, E. N. (1966). The arteries of the human kidney. *Journal of Anatomy*, **100**, 881-894.

Gray, H. (1973). *Anatomy*, 35th ed., London: Longman.

Hodson, J. (1972). The lobar structure of the kidney. *British Journal of Urology*, **44**, 246-261.

Löfgren, F. (1949). *Das topographische System der Pyramiden der Menschenniere*. Lund: Gleerup.

Potter, E. (1972). *The Normal and Abnormal Development of the Kidney*. Chicago: Year Book Medical Publishers, pp. 2 *et seq.*

Sutton, D. (1969). *A Textbook of Radiology*. Edinburgh: Livingstone, pp. 767-758.

Symington, J. (1914). In: Quain, J., *Elements of Anatomy*, 11th ed., Vol. 2, part 2, London: Longman, pp. 212 *et seq.*

Testut, L. (1895). *Traité d'anatomie humaine*, vol. 3, Paris: Doin.

The Authors

H. Fine, FRCSE, Consultant Urologist, King Edward VIII Hospital, Durban.

E. N. Keen, MD(Cape Town), FRCS, Professor of Anatomy, Medical School, Observatory, Cape Town.

British Journal of Urology (1976), **48**, 170 ©

Short Case Report

Peritoneal Tuberculosis with Ureteric Obstruction, Mimicking Retroperitoneal Fibrosis

Case Description

An 18-year-old male presented with colicky lower abdominal pain and vomiting. He had a weight loss of 2 stones (12·7 kg) and a dry cough. A diagnosis of appendicitis was made and at operation, straw-coloured fluid was aspirated from the peritoneal cavity. There were multiple nodules, 2-3 mm diameter, covering the caecum, terminal ileum and parietal peritoneum. Histology revealed non-caseating granulomata.

Antituberculous chemotherapy was started, a chest X-ray showed an apical mass with hilar enlargement and an intravenous urogram revealed bilateral ureteric obstruction and dilated renal pelves; the ureters were drawn in towards the midline and the psoas shadows were absent (Fig.). This appearance suggested retroperitoneal fibrosis and a laparotomy was performed, at which there was no sign of retroperitoneal fibrosis, although the left ureter was bound down with vascular adhesions beneath the rectosigmoid junction.

Biopsy of the peritoneal nodules now showed caseating tuberculosis.

Recovery was uneventful.

Comment

Peritoneal tuberculosis, without a localised enteric lesion is usually assumed to be haematogenous in origin (Nice, 1950; Fedotin and Brewer, 1972). Caseation in our case occurred during the 19 days separating the 2 operations. This "anergic tubercle", may be being viewed prior to development of hypersensitivity or in the presence of overwhelming infection with immunological paralysis and hyposensitisation.

The urogram suggested retroperitoneal fibrosis, but medial placement of the ureters has been described as a normal variant (Saldino and Palubinskas, 1972).

It is suggested that the mild degree of back pressure in our case was due to vascular adhesions at the pelvic brim, associated with tuberculous peritonitis, and that the medial deviation of the ureter was a normal variant, the features combining to mimic retroperitoneal fibrosis.

We would like to thank Dr F. E. Dische for help with the microscopy and Mr E. R. Howard and Mr D. A. Packham for permission to report this case.

P. G. Bentley and D. R. Higgs
Department of Surgery, Dulwich Hospital, London

References

Fedotin, M. S. and Brewer, D. L. (1972). Non-caseating tuberculous peritonitis. *Archives of Internal Medicine*, **130**, 920-922.

Nice, C. M., Jr. (1950). The pathogenesis of tuberculosis. *Diseases of the Chest*, **17**, 550-560.

Saldino, R. M. and Palubinskas, A. J. (1972). Medial placement of the ureter: a normal variant which may simulate retroperitoneal fibrosis. *Journal of Urology*, **107**, 582-585.

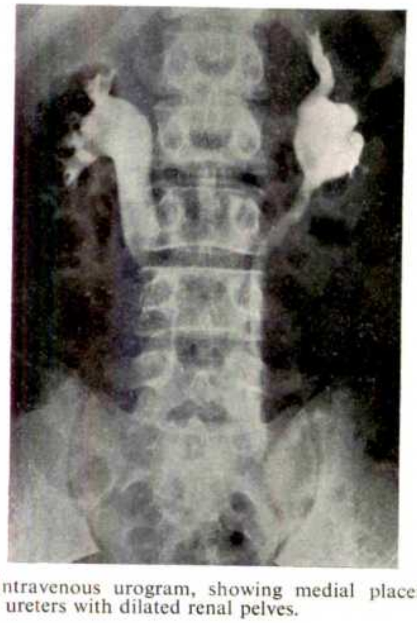


Fig. Intravenous urogram, showing medial placement of the ureters with dilated renal pelves.

British Journal of Urology (1976), **48**, 171–174 ©

Crossed Renal Ectopia with Colic
A Clinical Clue to Embryogenesis

D. G. ROMANS, M. A. S. JEWETT and C. J. ROBSON
Department of Surgery (Urology), Toronto General Hospital, Toronto, Ontario, Canada

Crossed renal ectopia is a relatively rare congenital anomaly. It has been extensively reviewed (Abeshouse, 1947; McDonald and McClellan, 1957) and a spectrum of renal and extrarenal pathology including renal and ureteral calculi described.

The precise pathogenesis of the crossed ectopia has been a subject of conjecture and debate. Generally accepted theories have largely been concerned with the irregular and often bizarre fusion anomalies commonly found in these cases and, for the most part, have been based on observations of anatomical relationships within the embryonic and adult pelvis. Consideration has been given to abnormalities of the ureteric bud, including those of location, rotation, and of direction and rate of growth, to vascular impediments to normal development, and to certain environmental factors related to other intrapelvic structures. No apparent correlation of clinical symptoms with anatomic pathology, however, has appeared thus far.

Of the 9 cases of crossed renal ectopia in the records of the Toronto General Hospital between 1943 and 1973, 3 cases have presented with classical ureteral colic. In 2 of these, the associated stone was in the crossed ureter with accompanying pain lateralised to the anephric side. These 2 patients and 4 cases from the literature revealing clinical clues to embryogenesis are presented.

Case Reports

Case 1. A 26-year-old male was admitted to the Toronto General Hospital on 24th January 1971 with a 3-hour history of severe colicky left flank and left lower quadrant (LLQ) pain radiating into the left testicle but unaccompanied by other urinary symptoms. The abdomen was tender periumbilically, with referred pain in the LLQ upon palpation in the contralateral (RLQ) side. No masses were palpable. The urine was positive for blood, and a subsequent intravenous pyelogram (Fig. 1) showed a left crossed renal ectopia with fusion, some slight delay in excretion in the ectopic kidney, and hold-up of dye behind a radiopaque stone in the left mid-pelvic ureter. The patient became asymptomatic within 12 hours of conservative therapy and was discharged with the stone unmoved. A 4-month follow-up KUB revealed no evidence of the obstructing calculus.

Case 2. A 37-year-old male was seen in the Emergency Department of the Toronto General Hospital on 14th February 1974 with a 2-hour history of severe colicky left costovertebral angle pain without radiation, one which over the next hour began to move into the left flank with radiation to the left groin and testis. Several hours prior to presentation, the patient had experienced some urgency with total dysuria and had passed slightly pink urine. On examination, moderate tenderness with slight guarding was found over the left renal angle and flank and in the LLQ. Intravenous pyelography (Fig. 2) revealed a left crossed ectopia with fusion and partial obstruction of the crossed collecting system. A small calculus was seen at the left ureterovesical junction but passed spontaneously during the procedure and was recovered to show calcium oxalate by analysis. Subsequent biochemical studies were unremarkable and the patient has remained asymptomatic to the present.

Discussion

Fundamental to a consideration of pain as relating to the pathogenesis of crossed renal ectopia is an understanding of normal embryologic events and of the innervation of both ureter and kidney. About the 5 mm stage of embryonic life, the ureteric bud appears as an outgrowth on the dorsal surface of the Wolffian duct and, during the 5 to 7 mm stages, shifts dorsilaterally to

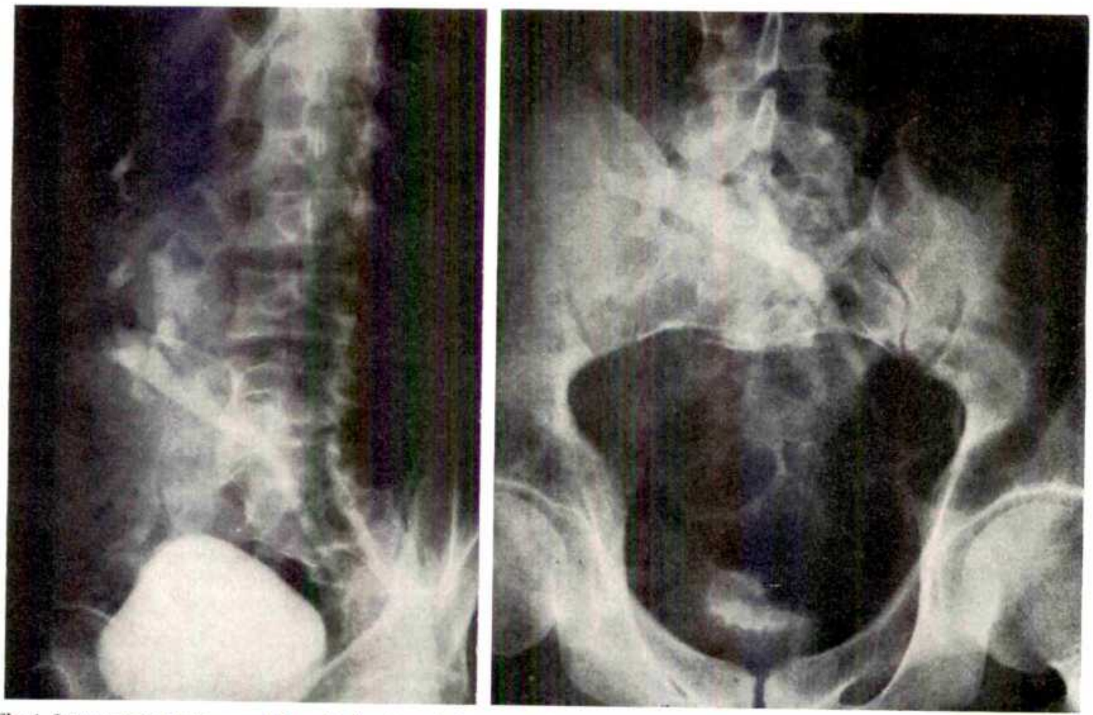


Fig. 1. Intravenous pyelogram (Case 1) showing a left crossed fused ectopia with hold-up of dye behind a small radiopaque stone within the left mid-pelvic ureter.

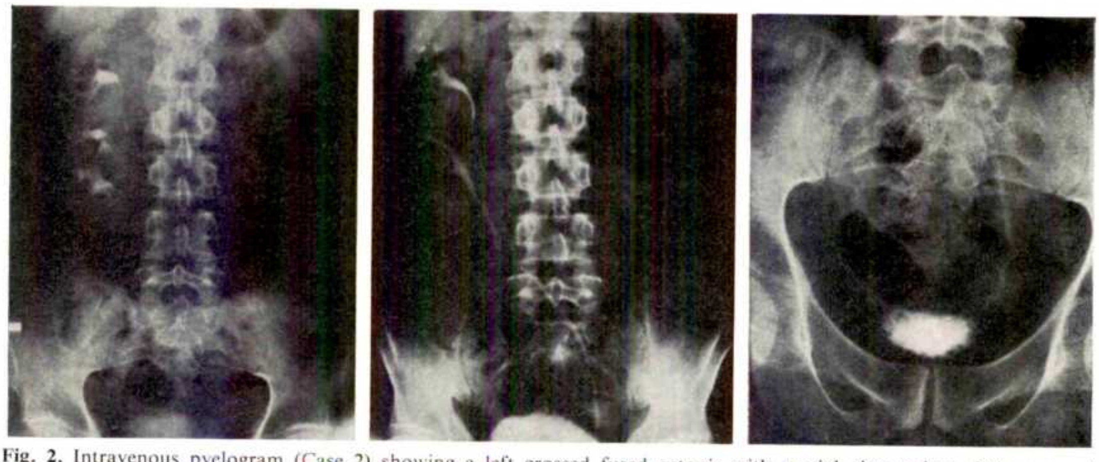


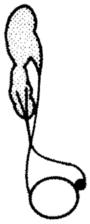
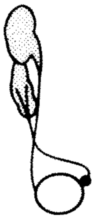
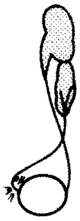
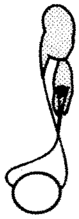
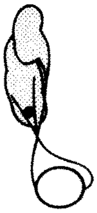
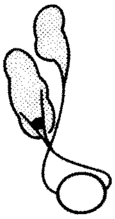
Fig. 2. Intravenous pyelogram (Case 2) showing a left crossed fused ectopia with partial obstruction of the crossed collecting system.

become surrounded by the metanephric blastema. Since the ureteric bud seems to have a strong organising effect on the developing nephrogenic cell mass, it could, in cases of crossed ectopia, migrate to the opposite side during this time, a distance of less than 1 mm, influence the contralateral blastema and ascend to an almost normal position by usual mechanisms.

Considering first those cases having colic associated with a ureteral calculus, it is known that overdistension of the ureter and, to a lesser extent, spasm of its muscular coat related to an intraluminal stone are adequate stimuli to produce colic, a pain that is referred to the cutaneous areas

Table

Crossed Renal Ectopia with Colic: Cases revealing Clinical Clues to Embryogenesis

Author	Age/Sex	Clinical findings	Pyelographic findings	Ectopia
Romans *et al.* 1975	26 M	L flank to LLQ and L testis colic		L crossed with fusion
Romans *et al.* 1975	37 M	L flank to LLQ and L testis colic		L crossed with fusion
Culp 1944	31 M	hypogastric to R testis colic		R crossed with fusion
Beer and Ferber 1937	24 M	L lumbar pain × 2 years		R crossed with fusion
Abeshouse 1946	33 M	hypogastric, RLQ pain × 5 months		L crossed with fusion
Beer and Ferber 1937	45 M	R lumbar pain × 2 years		L crossed without fusion

innervated by the same segments of the spinal cord as is supplied by the ureter, mainly T_{11}-L_2 (Mitchell, 1935). Since the ureteric bud with its nerve supply develops from the usual side irrespective of the crossed ectopia, and ultimately becomes the definitive ureter and renal pelvis, in the event of a stone lodging anywhere along the ureter from the renal pelvis to the bladder orifice one should expect the associated colic to lateralise to the side of embryologic origin. This is, in fact, a uniform finding in the 3 cases of this type (cases 1, 2 and 3) collected.

Secondly, one must consider those cases in which the crossed ectopia was associated with an obstructing calculus at the ureteropelvic junction. Although *Gray's Anatomy* describes the renal plexus of nerves as extending into the kidney along the renal arteries to subserve, in the main, vasomotor function, and makes no mention of capsular innervation, it is generally felt that the constant dull aching loin pain so typical of kidney distension, whether due to inflammatory oedema such as occurs in acute glomerulonephritis, or to a hydronephrosis, is caused by stretching of a sensitive capsule, a derivative of the metanephric blastema and not of the ureteric bud. From this basis it is proposed that, if the ureteric bud were to cross the midline to influence the contralateral blastema, with subsequent development, the symptoms associated with the hydronephrosis would be uncrossed, that is, on the same side as the renal mass. Indeed, this is the case in the 3 patients (cases 4, 5 and 6) previously reported to have a crossed renal ectopia complicated by chronic ureteropelvic junction obstruction, a finding which reaffirms the theory of ureteral, and not renal, migration as the abnormal event. No attempt, however, can be made from this clinical study to define further the precise aetiology of the ureteric crossover.

Summary

A clinicopathologic correlation of 2 patients with crossed renal ectopia presenting with ureteric colic and 4 cases collected from the literature is presented.

The correlation serves to reaffirm the theory of ureteral and not renal, migration as the primary aberration resulting in this defect.

The kind advice of Dr J. W. A. Duckworth, Professor of Anatomy, University of Toronto, is gratefully acknowledged.

References

ABESHOUSE, B. S. (1947). Crossed ectopia with fusion: review of literature and a report of four cases. *American Journal of Surgery*, **73**, 658-683.

BEER, E. and FERBER, W. F. L. (1937). Crossed renal ectopia. *Journal of Urology*, **38**, 541-561.

CULP, O. S. (1944). Renal ectopia: report of six cases. *Journal of Urology*, **52**, 420-429.

MCDONALD, J. H. and MCCLELLAN, D. S. (1957). Crossed renal ectopia. *American Journal of Surgery*, **93**, 995-1002.

MITCHELL, G. A. G. (1935). The innervation of the kidney, ureter, testicle, and epididymis. *Journal of Anatomy*, **70**, 10-32.

The Authors

D. G. Romans, MD, Intern.
M. A. S. Jewett, MD, FRCS(C), Chief Resident in Urology.
C. J. Robson, MD, FRCS(C), FACS, Professor of Urology.

Correspondence: Dr C. J. Robson, Department of Urology, Toronto General Hospital, Toronto, Ontario M5G 1L7, Canada.

British Journal of Urology (1976), **48**, 175-176 ©

Hydronephrosis and Polycythaemia

A. SRIMAN NARAYANA, F. GALLAGHER, D. G. KELLY and F. A. DUFF

Department of Urology, St Vincent's Hospital, Dublin

Case Reports

Case 1. T. L., a 51-year-old man, presented to the Neurosurgical Unit with a history of dimming of vision, aphasia and transient right-sided hemiparesis. Blood pressure on admission was 210/100 mm Hg. Physical examination otherwise was normal.

Investigations

Full blood count showed a haemoglobin of 18·8 g%; erythrocytes $6{\cdot}77 \times 10^6$/cumm; PCV 56%; MCHC 35·5% and MCV 85 cumicrons; leucocytes 4,512/cumm; ESR 1 mm/hr. Platelet count was normal. Total blood volume 6,900 ml or 92 ml/kg; red cell volume 48 ml/kg; plasma volume 44 ml/kg. Chest X-ray, PO_2 and O_2 saturation, were all within normal limits.

Secondary polycythaemia was diagnosed and venesection was performed. IVP showed a non-functioning left kidney. A left selective renal angiogram showed a small tapered-off renal artery. The left kidney was explored and an empty hydronephrotic sac, distendable up to 2 L was found. Immediately postoperatively his blood pressure was recorded at 100/70 mm Hg and within 7 days it had stabilised at 120/80 mm Hg. Haemoglobin estimations immediately postoperatively and at 7 days were 12·0 and 12·5 g% respectively. Subsequent out-patient follow-up at 6 and 18 months showed blood pressure readings of 120/80 mm Hg and haemoglobin levels of 12·5 and 13·0 g%.

Case 2. J. N., a 43-year-old man, was admitted to the Urology Unit for investigation of right loin pain and haematuria. Except for a plethoric facies physical examination including blood pressure was normal.

Investigations

Full blood count showed a haemoglobin of 19·0 g%; erythrocytes $6{\cdot}9 \times 10^6$/cum; PCV 58%; MCHC 32%; MCV 87 cumicrons; leucocytes 4,527/cumm; ESR 1 mm/hour. Platelet count was normal. Total blood volume 9,700 ml or 108·4 ml/kg. Red cell volume 61·7 ml/kg; plasma volume 46·7 ml/kg. Chest X-ray, pO_2 and O_2 saturation, were all within normal limits.

Secondary polycythaemia was diagnosed and venesection performed. IVP showed a mass in the lower pole of the right kidney. The right kidney was explored and a lower pole heminephrectomy performed for a hydronephrotic lower segment. Postoperatively his blood pressure continued in the normal range. Haemoglobin estimations immediately and at 7 days post-operatively were 12·0 g% on both occasions. Out-patient follow up at 6 and 18 months showed haemoglobin levels of 13·0 and 13·5 g% respectively and normal blood pressure readings.

Discussion

Polycythaemia vera has long been recognised as a disorder of proliferation of bone marrow. The cardinal feature of this disorder is the fact that it is a panmyelopathy.

In secondary polycythaemia the increased proliferation of the bone marrow is limited to the erythrocyte series. Secondary polycythaemias are produced by the appropriate response of a normal bone marrow to an increased intensity of the normal stimulus, erythropoeitin. In a sense this is therefore, not a haematological disease and the cause of increased erythropoeitin production must be sought outside the bone marrow. The increase in erythropoiesis may be the response to a physiological or appropriate increase in erythropoietin production or to a pathological or inappropriate increase in erythropoietin production, as in our cases. Thus many fundamentally different conditions are associated causally with secondary polycythaemia. Furthermore, while it is true that in most cases of secondary polycythaemia the leucocyte and platelet counts are normal, a number of important exceptions to this exist in the literature. These exceptions have either been ignored or the renal lesions have been considered to be coincidental findings in a patient with polycythaemia vera (Ways *et al.*, 1961). In a few of these patients who had polycythaemia—with leucocytosis, thrombocytosis or splenomegaly— and an associated renal lesion, nephrectomy was followed by a reversal of the polycythaemia (Lawrence and Donald, 1959). This suggests that the renal lesion was the cause of the polycythaemia in these cases.

Benign renal lesions have been described as the cause of secondary polycythaemias but more often the cause is renal cell carcinoma. Benign lesions include solitary cysts, multiple cysts, polycystic disease but only rarely had hydronephrosis been reported as the cause.

In view of the common association between secondary polycythaemia and renal lesions it behoves the clinician to search for such lesions when a diagnosis of secondary polycythaemia is made.

Summary

2 cases of secondary polycythaemia apparently caused by hydronephrosis are described.

The polycythaemia resolved following nephrectomy in each case.

References

BERGER, L. and SINKOFF, M. W. (1957). Systemic manifestations of hypernephroma. A review of 273 cases. *American Journal of Medicine*, **22**, 791-796.

FRIED, W. and GURNEY, C. W. (1968). The erythropoietic stimulating effect of androgens. *Annals of the New York Academy of Science*, **149**, 356-360.

GURNEY, C. W. (1973). *Pathogenesis of polycythaemias*. In: Polycythaemia, Theory and Management. Ed. H. Klein, Springfield, Ill., Thomas, pp. 43-60.

LAWRENCE, J. H. and DONALD, W. G. (1969). Polycythemia and hydronephrosis or renal tumors. *Annals of Internal Medicine*, **50**, 959-969.

WAYS, P., HUFF, J. W., KOSMALER, C. H. and YOUNG, L. E. (1961). Polycythaemia and histologically proven renal disease. *Archives of Internal Medicine*, **107**, 154-162.

The Authors

A. Sriman Narayana, MS, FRCSI (now Senior Registrar, Iowa University Hospital, Iowa, USA).
F. Gallagher, MB, Medical SHO.
D. G. Kelly, MCH, FRCSI, Consultant Urologist.
F. A. Duff, MCH, FRCSI, Consultant Urologist.

British Journal of Urology (1976), **48**, 177-182 ©

A Simple Method for Studying the Formation of Calcium Oxalate

D. JUNE SUTOR
Department of Chemistry, University College, London

Nucleation and crystal growth are of importance in the formation of urinary and other pathological stones because these deposits consist predominantly of crystalline material. Information about these phenomena and factors which promote or inhibit them is therefore vital to our understanding of the process of stone nucleation and growth. Much of the recent research work into the formation of upper urinary tract stones containing calcium has involved the recognition, isolation and identification of urinary substances which inhibit crystal growth and an assessment of the role of these compounds in the formation of stones. Several methods have been developed for studying these inhibitors but many are either time-consuming or involve expensive or specialised equipment (see for example Thomas and Tomita, 1967; Sutor, 1969; Robertson, Peacock and Nordin, 1973). A simple system for studying crystallisation would therefore be useful in investigating the formation of stone constituents. This paper describes such a method and its application to the formation of calcium oxalate. Calcium oxalate was chosen because it is the most abundant and frequently occurring constituent of upper urinary tract calculi in the industrialised countries and it is commonly found in bladder stones from technically developing countries (Sutor, Wooley and Illingworth, 1974). The method can, however, be equally well applied to the formation of many other substances.

Method

The formation of calcium oxalate was followed using a nephelometer to measure the turbidity of the suspensions produced by mixing the precipitating reagents.

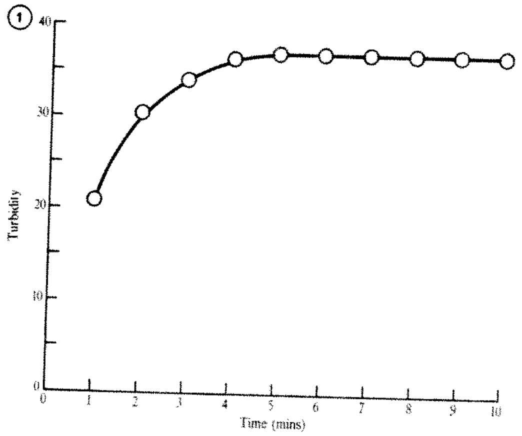
In the Corning-EEL nephelometer head used in these experiments, a beam of light passes up through the base of the test-tube containing the suspension. Light scattered by particles in the liquid is reflected on to a photocell and fed into a Unigalvanometer. The turbidities are presented on a linear scale and are relative to the perspex standard used to set the maximum deviation (100) on the galvanometer. The sensitivity control used for this adjustment can be varied considerably and at high sensitivities, barely visible precipitates can be measured. Standards of different opacities to cover the sensitivity range available were made by shot-blasting perspex rod.

For nephelometric work to be successful, the compound must have a low solubility and precipitation must be undertaken in dilute solutions with a concentration of around 100 mg/l (Yoe 1929).

Suspensions of calcium oxalate satisfying these conditions can be produced very easily. A total volume of 10 ml of solution was required for the nephelometer tube. In order to study precipitation in the presence of different compounds, measurable precipitates were produced by using 1 to $2\frac{1}{2}$ ml of a solution of calcium chloride dihydrate (5 mmol/l) and an equal quantity of freshly prepared sodium oxalate solution (5 mmol/l), the rest of the 10 ml being water, a suitable control or the test material. The technique consisted in adding say $2\frac{1}{2}$ ml of the calcium chloride dihydrate solution to the test-tube followed by 5 ml of water or the control solution and mixing them by inversion. The solution which should be clear was then used to zero the galvanometer. With the chosen standard, the sensitivity control on the galvanometer was adjusted so that a reading of 100 was showing on the linear scale. $2\frac{1}{2}$ ml of the sodium oxalate solution was added to the test-tube using a fast-flowing pipette,[1] the time noted and the solutions mixed by inversion. Readings of the turbidity were taken every minute for a chosen period of time, say

---

[1] Tests were made on whether it was preferable to inject or stir in the sodium oxalate rather than add it quickly and then mix the solutions. The different techniques produced negligible differences in the results so the last was chosen because of its simplicity.



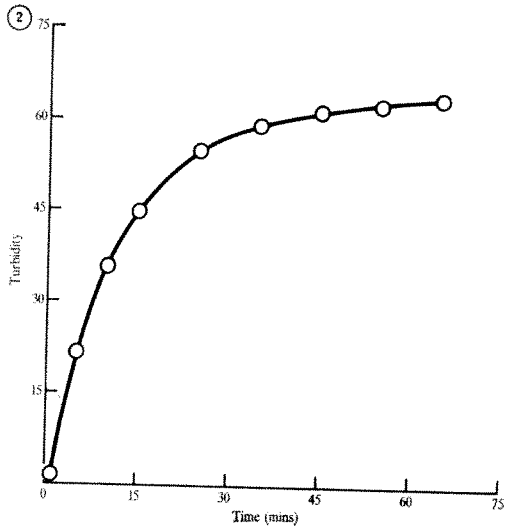


Fig. 1. The turbidity of calcium oxalate suspensions measured at 1-min intervals after mixing calcium chloride dihydrate and sodium oxalate solutions in water so that the calcium and oxalate concentrations were 1·25 mmol/l.

Fig. 2. The turbidity of calcium oxalate suspensions measured at 5- and then 10-min intervals after mixing calcium chloride dihydrate and sodium oxalate solutions in water so that the calcium and oxalate concentrations were 0·5 mmol/l. Perspex standard used for setting maximum deflection on the galvanometer approximately one-fifth of the turbidity of that used for data in Figs. 1, 3 and 4.

10 min. Between each reading the tube was removed from the nephelometer head so that the reaction was not accelerated by heat generated in the head, and the test-tube was shaken. Usually 2 or 3 runs were made and a mean taken.

The experiments were then repeated using 5 ml of a solution containing the compound whose effect on the nucleation and formation of calcium oxalate was to be studied. The percentage amount of inhibition produced by the test material could then be calculated from the formula

$$\frac{R_C - R_T}{R_C} \times 100$$

where R_C was the reading given by the control at say 10 min and R_T was the reading given by the test solution after the same time interval.

Because the solubility of calcium oxalate increases rapidly in acid and alkaline solutions, the pH of experiments designed to test any inhibitory effect (other than that of pH) is preferably kept within the range 5·7 to 6·5. This was done by adjusting the pH of the test solutions. Buffering was not necessary as changes in pH during the formation of calcium oxalate under the conditions used were negligible. To allow for any increase in the solubility of calcium oxalate resulting from an increase in the ionic strength of the solution when the inhibitory power of electrolytes was tested, the effect of sodium chloride was examined.

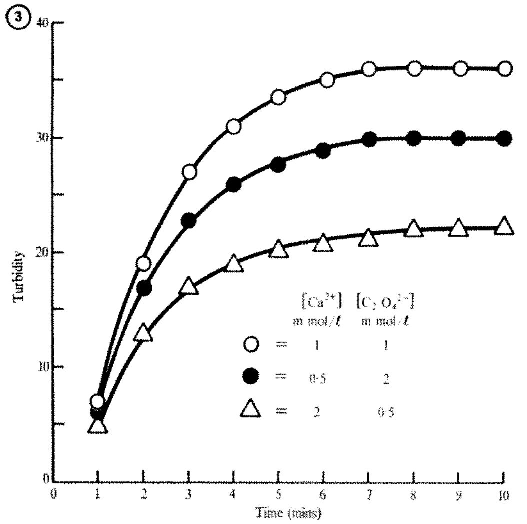
The substances chosen for the test solutions were citrate which is known to form a soluble complex with calcium, and heparin which is thought to be adsorbed on to crystal faces and so prevent further growth on them.

Measurements were also made on the amount of calcium oxalate produced by varying the relative concentrations of calcium and oxalate ions but keeping their ion product the same.

Results

Formation of Calcium Oxalate

When dilute solutions of calcium chloride dihydrate and sodium oxalate were mixed, the amount of material formed as measured by the turbidity of the solution, gradually increased with time until a maximum was reached. This gradual increase in the amount of precipitate could also be followed visually. If 2½ ml of each of the precipitating reagents and 5 ml of water were used, that is the concentration of calcium and oxalate ions in the 10 ml was 1·25 mmol/l, the curve representing the plot of turbidity against time rose steeply and reached a maximum after a few minutes



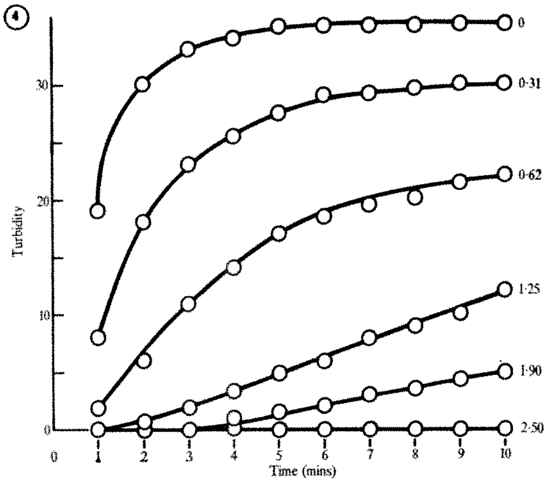


Fig. 3. The turbidity of calcium oxalate suspensions plotted at 1-min intervals after mixing calcium chloride dihydrate and sodium oxalate solutions in water. The ion product of calcium and oxalate was 1×10^{-6} mol^2 litre^{-2} but the relative concentrations of each ion were varied.

Fig. 4. The turbidity of calcium oxalate suspensions plotted at 1-min intervals after mixing calcium chloride dihydrate and sodium oxalate solutions in the presence of sodium citrate. Calcium and oxalate concentrations were both 1·25 mmol/l. and the concentration of sodium citrate (mmol/l) is given on each curve.

(Fig. 1). The turbidity was the same after 2 hours, the longest time over which measurements were made. When only 1 ml of the precipitating reagents and 8 ml of water were used, that is the concentration of calcium and oxalate ions in the 10 ml was 0·5 mmol/l, detectable nucleation was delayed for a few minutes (Fig. 2). After that the curve of turbidity against time rose gradually and a maximum was not reached for over an hour.

Provided that measurements were made under the same conditions and at the same temperature, the reproducibility of the results was particularly good for the higher concentrations of calcium and oxalate. Some variations, however, could be experienced for the smaller concentrations when a high sensitivity setting on the galvanometer was used. In all experiments, a standard curve was determined daily and checked throughout the day.

At added concentrations of sodium chloride equivalent to 37 mmol/l in the presence of 1·25 mmol/l of calcium and oxalate and to 1·2 mmol/l in the presence of 0·5 mmol/l of calcium and oxalate, there was no alteration in the respective curves of turbidity against time. The ionic strength of these solutions was very much greater than any used in testing the action of inhibitors, so that any decrease in the amount of calcium oxalate formed in these tests cannot be attributed to the ionic strength of the solution.

Effect of varying the Relative Concentrations of Calcium and Oxalate

When the relative concentrations of calcium and oxalate were varied but the ion product was kept constant, the amount of precipitate produced also varied. The results for [calcium] [oxalate] $= 1 \times 10^{-6}$ mol^2 litre^{-2} are plotted in Figure 3. The turbidity was greatest when the concentration of calcium and oxalate were both 10^{-3} mol/l. As expected it was reduced when the oxalate concentration was 4 times that of calcium (2×10^{-3} mol/l and $0{\cdot}5 \times 10^{-3}$ mol/l respectively). The lowest value was obtained when the concentration of calcium was 4 times that of oxalate. The same phenomenon was observed for calcium and oxalate ion products of 4×10^{-6}, $1{\cdot}5 \times 10^{-6}$ and $2{\cdot}5 \times 10^{-7}$ mol^2 litre^{-2}.

⑤

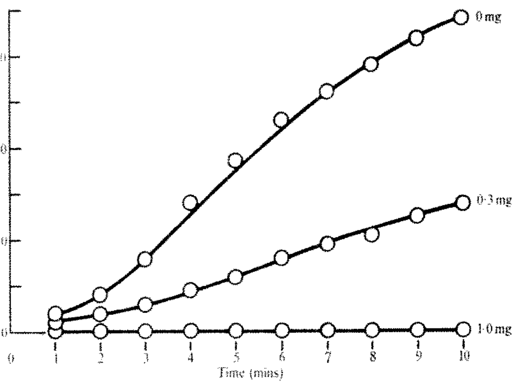


Fig. 5. The turbidity of calcium oxalate suspensions plotted at 1-min intervals after mixing calcium chloride dihydrate and sodium oxalate solutions in the presence of heparin. Calcium and oxalate concentrations were both 0·5 mmol/l and the amount of heparin present is shown on each curve. Perspex standard used for setting maximum deflection on galvanometer appoximately one-fifth of the turbidity of the standard used for data in Figs. 1, 3 and 4.

Effect of Different Compounds on the Formation of Calcium Oxalate

(*a*) *Sodium Citrate*

The effect of sodium citrate on the formation of calcium oxalate in shown in Figure 4. In all cases 2½ml of each of the precipitating reagents were used and 5 ml of water or sodium citrate solution. When sodium citrate was added, the amount of calcium oxalate formed decreased until at a concentration of 2·5 mmol/l., the sodium citrate completely inhibited the precipitation of calcium oxalate during the 10-min period that observations were made.

(*b*) *Heparin*

Calcium oxalate was precipitated using 1 ml of calcium chloride dihydrate, 1 ml of sodium oxalate and 8ml of water. Then the water was replaced by aqueous solutions of varying concentrations of heparin. Again the amount of calcium oxalate formed was reduced in the presence of heparin, and 100% inhibition was produced by approximately 1 mg of this material (Fig. 5).

Discussion

The formation of calcium oxalate has been followed using a nephelometer to measure the light scattered by suspensions produced when dilute solutions of calcium chloride dihydrate and sodium oxalate were mixed. The power of turbid solutions to disperse light depends on the number of particles present and their size. These factors are unknown and have not been measured because conditions identical with those under which the turbidities were determined in the nephelometer cannot be reproduced in say a Coulter Counter which requires the particles to be suspended in an electrolyte like sodium chloride. However, the reproducibility of the measurements was good, especially for the more concentrated solutions (calcium and oxalate concentrations around 1·25 mmol/l), suggesting that, under the same experimental conditions, a closely similar distribution of the number and size of the particles was produced. Furthermore, the turbidity of the solutions was reduced when substances were introduced which are known inhibitors of calcium oxalate formation. The turbidities can therefore be assumed to give at least a semi-quantitative estimation of the amount of calcium oxalate present.

By plotting the turbidities measured every minute after mixing the precipitating reagents, the rate of reaction was followed. This was rapid for calcium and oxalate concentrations of 1·25 mmol/l. but slow when the concentrations were only 0·5 mmol/l. Nucleation was instantaneous on mixing in the former case but it was frequently delayed for a minute in the latter.

Of interest are the different amounts of calcium oxalate formed when the relative concentrations of calcium and oxalate were varied but their ion product kept constant. Less material was apparently produced when calcium was in excess of oxalate than vice versa. This suggested that calcium oxalate might form a soluble complex in excess calcium. Finlayson, Roth and DuBois (1973) have also postulated the existence of a similar complex.

When substances like sodium citrate and heparin which are known to inhibit the formation of calcium oxalate were present, the curves in each system were reduced in height. The more inhibitor present, the lower the curve, until at a certain concentration, no material was formed. To test possible inhibitory compounds, the formation of calcium oxalate need only be followed over a short period of time even though complete precipitation would not have occurred in dilute solutions.

The two compounds tested are thought to inhibit calcium oxalate formation in different ways. Citrate forms a soluble complex with calcium but it has been suggested that heparin is adsorbed on to certain crystal faces so preventing further growth on them (Crawford, Cremarty and Alexander, 1968). The nephelometric method cannot distinguish between these different modes of action, but this is true of most systems since a reduction in the amount of material formed or in crystal growth can be attributed to both types of inhibitor. The advantages of the technique described here are that it is quick and simple, it can be used to study nucleation and only a small amount of material is required.

Summary

The nucleation and crystal growth of calcium oxalate were studied under different conditions using a nephelometer to measure the turbidities of suspensions produced when dilute solutions of calcium chloride dihydrate and sodium oxalate were mixed.

The amount of material produced was less when calcium was in excess of oxalate than vice versa.

For equimolar amounts of the precipitating reagents the rate of formation of calcium oxalate was rapid when calcium and oxalate concentrations were 1·25 mmol/l. but slow when they were 0·5 mmol/l.

Sodium citrate and heparin inhibited nucleation and crystal growth and at certain concentrations prevented nucleation for the duration of the experiment.

The method is simple and quick and requires only a small amount of material.

This work was financed by the Medical Research Council.

References

CRAWFORD, J. E., CREMARTY, E. P. and ALEXANDER, A. E. (1968). The effect of natural and synthetic polyelectrolytes on the crystallisation of calcium oxalate. *Australian Journal of Chemistry*, **21**, 1067-1072.

FINLAYSON, B., ROTH, R. and DUBOIS, L. (1973). Calcium oxalate solubility studies. In *Urinary Calculi*, Ed. L. Cifuentes Delatte, A. Rapado and A. Hodgkinson. Basel, Karger, pp. 1-7.

ROBERTSON, W. G., PEACOCK, M. and NORDIN, B. E. C. (1973). Inhibitors of the growth and aggregation of calcium oxalate crystals *in vitro*. *Clinica Chimica Acta*, **43**, 31-37.

SUTOR, D. J. (1969). Growth studies of calcium oxalate in the presence of various ions and compounds. *British Journal of Urology*, **41**, 171-178.

British Journal of Urology (1976), **48**, 183–192 ©

Circumcaval Ureter: A Report of Four Cases in Children with a Review of the Literature and a New Classification

M. M. KENAWI and D. INNES WILLIAMS
Institute of Urology and St. Peter's Hospitals, London

Circumcaval ureter is a well-recognised congenital anomaly commonly causing ureteric obstruction but it is seldom reported in childhood: only 17 out of 162 cases collected from the literature were recognised before 12 years of age. To these we now add 4 more. Our experience suggests that the disorder is easily recognisable in childhood and readily correctable at this stage. Later in life it is clear that progressive damage has usually occurred and many reports speak of operative difficulties or of poor renal and ureteric recovery. However, a few adult cases show no obstruction and suffer no symptoms, so that if early operative treatment is to be advised it is important to be able to distinguish those with a good prognosis from those with a poor one. With these needs in mind the literature has been reviewed and 2 anatomical varieties of the disorder with predictive features have been distinguished. In addition it is recognised that true retrocaval ureter exists, in which the ureter runs its length behind the cava instead of encircling it: such cases have been described by Lerman, Lerman and Lerman (1956), Dreyfuss (1959), Peisojovich and Lutz (1969): they clearly fall into an altogether different category and are not further discussed.

Case 1. C. U. had a tracheo-oesophageal fistula with oesophageal atresia repaired a few hours after birth. He subsequently developed heart failure and was found to have atrial and ventricular septal defects as well as a patent ductus arteriosus. His pulmonary artery was banded and his patent ductus ligated at 1 month of age. At operation he was found to have an accessory left superior vena cava. A further angiocardiographic study at 7 years of age demonstrated a right hydronephrosis with a normal left kidney. Intravenous urography confirmed that a hydronephrosis was present with upper hydroureter of the reversed J form (Fig. 1a) Circumcaval ureter was diagnosed and at operation the presence of the anomaly was confirmed with dilatation of the ureter down to the retrocaval segment. The ureter was first divided as it appeared medial to the cava. There was no flow of urine from the cut end. It was then dissected free and divided at the point where it passed behind the cava. Urine flowed freely. An oblique ureteral anastomosis was performed over a T tube brought out through a ureterotomy incision below the anastomosis. Convalescence was uneventful and a subsequent intravenous urogram showed a return to normal (Fig. 1b). A year later the patient had his atrial and ventricular septal defects repaired and has progressed satisfactorily for the following 3 years.

Case 2. A. M. was found at birth to have a single umbilical artery, a patent ductus arteriosus and bilaterally enlarged kidneys. Intravenous pyelogram showed bilateral hydronephrosis and suggested pelviureteric obstruction. Exploration was undertaken without further diagnostic procedures. On the right side aberrant lower pole vessels appeared to be causing pelviureteric obstruction, but beyond this the ureter passed behind the vena cava and re-emerged medially on its anterior surface. The retrocaval segment was stenosed. The ureter was divided below the pelvi-ureteric junction, the narrow segment spatulated and anastomosed to the pelvis as a modified Hynes-Anderson pyeloplasty using a nephrostomy and splinting catheter. 10 days later the left kidney was operated upon. The hydronephrosis in this case appeared to be due to an upper ureteric stricture, some 2 cm below the pelviureteric junction. This was not involved in any vascular anomaly. The stricture was excised and ureteroureterostomy performed. 5 months later the patent ductus arteriosus was ligated. Post operative follow-up intravenous urography showed free drainage into the ureters and some residual dilatation of the kidneys. 7 years later progress has been satisfactory.

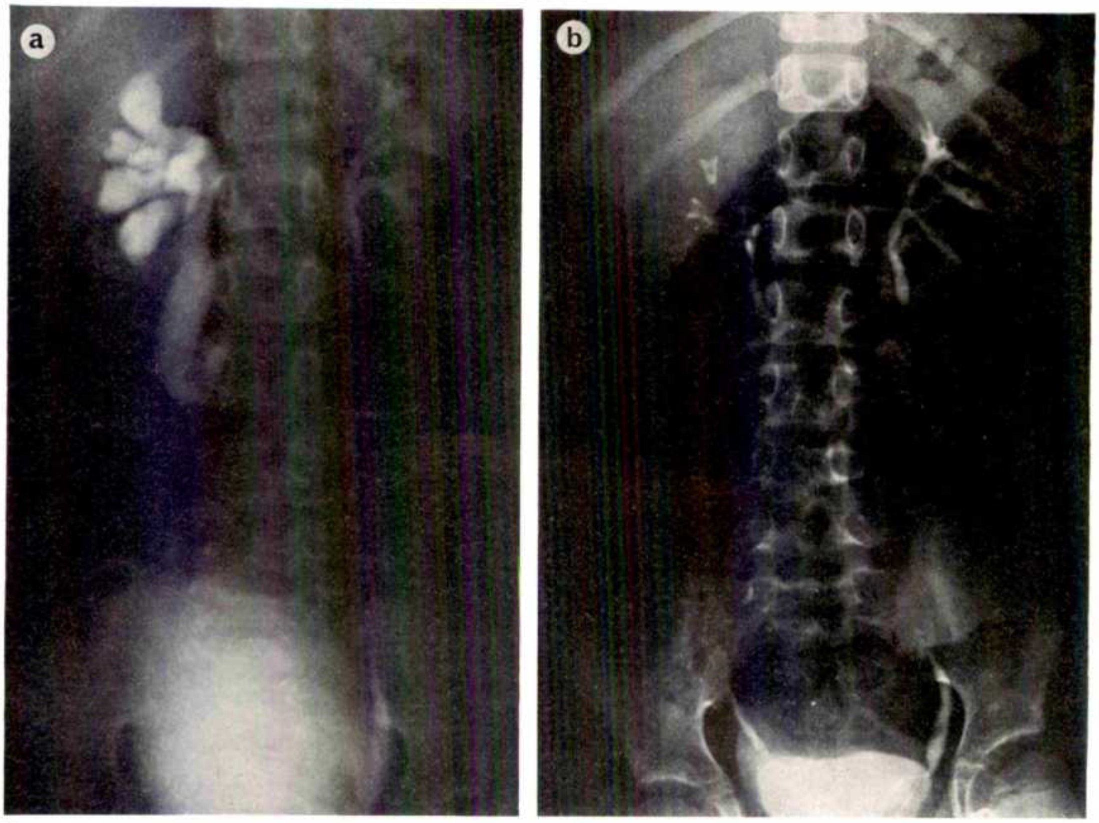


Fig. 1. (a) Intravenous urogram in Case 1, showing right hydronephrosis and upper hydroureter. The ureter curves upwards and medially at the level of the third lumbar vertebra in a reversed J shape. The retrocaval segment of the ureter is not filled; (b) Postoperative intravenous urogram in Case 1 showing good recovery.

Case 3. C. D. presented at the age of 12 years with a 4-month history of urinary infection and haematuria. Intravenous urography showed a right hydronephrosis and upper hydroureter with the characteristic reversed J form (Fig. 2a). At operation the ureter was found to course circumcavally, the retrocaval part was stenosed. It was excised and a ureteroureterostomy performed over a T tube. Convalescence was satisfactory and a follow-up pyelogram showed a good result (Fig. 2b). Subsequent progress has been satisfactory over 4 years.

Case 4. J. R. presented with haematuria at the age of 4 years. Intravenous urography showed right hydronephrosis and a hydroureter with the reversed J form. Circumcaval ureter was diagnosed and confirmed at operation. The ureter was divided 1 cm below the pelviureteric junction and the retrocaval segment was excised. An oblique end-to-end anastomosis was performed and satisfactory healing occurred. Subsequent pyelogram was normal.

Discussion

In reviewing the literature 184 well documented cases were collected. 22 of these were autopsy studies, many of which were fully reviewed by Antopol and Yelin (1939) and by Pick and Anson (1940) and will not be discussed further. An analysis was made of the remaining 162 cases.

Presentation

The patients most often presented during their third and fourth decade (Fig. 3), 114 were male, 41 were female and in 7 the sex was not stated. Most often the patients complained of renal pain or colic, with urinary infection as the next most common cause of presentation (Table I). Presenting symptoms were unrelated to the hydronephrosis in 17 patients suffering from such

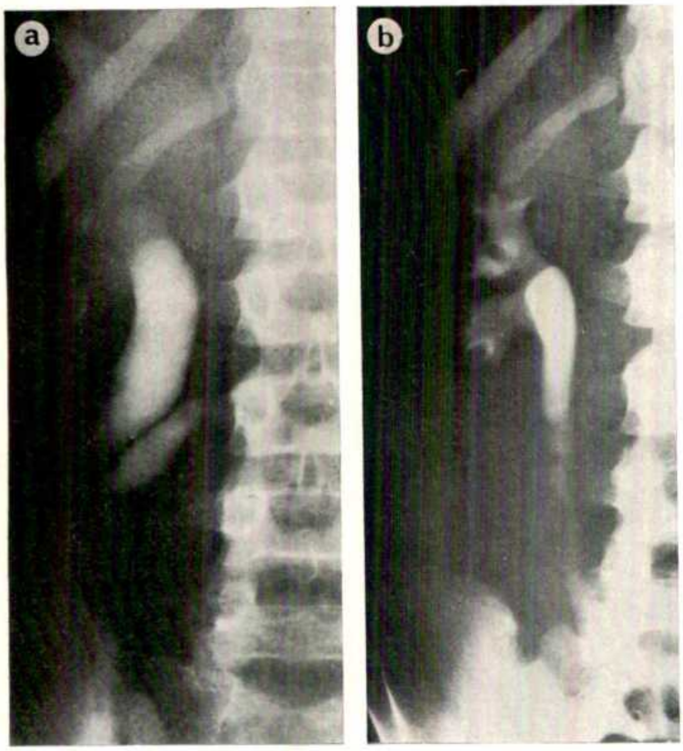


Fig. 2. (a) Preoperative intravenous urogram in Case 3 showing a right hydronephrosis and reversed J shaped hydroureter; (b) the postoperative pyelogram showing a marked improvement and a normal course to the ureter. The anastomotic site is somewhat irregular but there is free drainage through it.

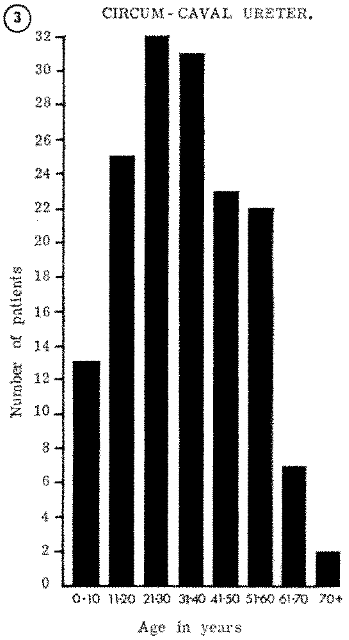
disorders as benign prostatic enlargement, hypospadias, enuresis, urethral stricture, epididymitis, pyrexia of unknown origin and Turner's syndrome. 1 was discovered at exploration for appendicitis.

Radiology and Classification

The common radiological appearance is as illustrated in our cases: we classify this as Type I circumcaval ureter (low loop). In the intravenous pyelogram the dilated upper right ureter is seen to descend from the renal pelvis and then to curve upwards and medially forming a reversed J appearance. The mid segment of the ureter where it lies behind the cava is not usually filled with opaque medium (Fig. 2) and in no less than 41·4% of the published films reviewed even the medial curvature of the ureter was not shown, so that the fully developed reversed J was depicted in only 58·6%. Retrograde pyelograms of the Type I circumcaval ureter show an S shaped outline, the curves more or less acute (Fig. 4). The level of the retrocaval segment was most frequently at the third lumbar vertebra. The relation of the retrograde ureteric catheter to the vertebral pedicles was studied in 138 cases. In 134 it lay medial to the pedicles reaching the midline in 29 and crossing it in 9. It overlay the pedicles in 3 cases and was lateral to them in only 1. As noted by Randall and Campbell (1935) a right oblique view will demonstrate the circumcaval ureter in contact with the lower lumbar vertebral column, whereas the normal ureter at this level falls forward and away from the vertebrae.

A separate type of circumcaval ureter could be identified in the literature; we shall term this Type II or the high loop (Fig. 4). Here the renal pelvis and upper ureter lie horizontally or very nearly so, so that the retrocaval element of the ureter is on the same level as the renal pelvis and on retrograde pyelography there is the appearance an inverted J. This picture was observed in 12 cases and separation of this group was justified by the fact that the pyelogram was otherwise

③



④

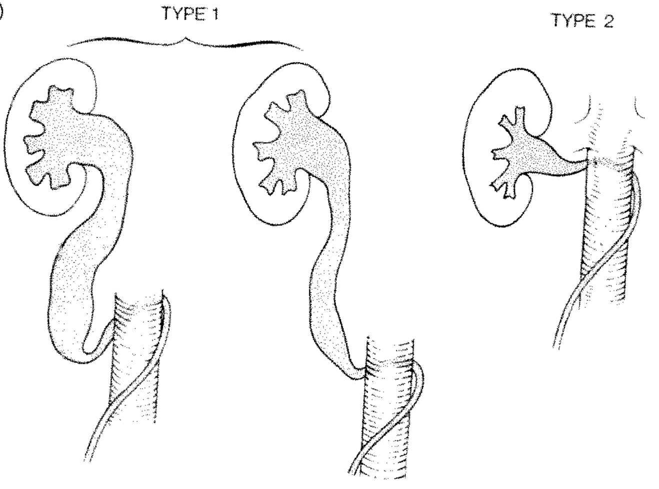


Fig. 3. The age incidence in 162 patients with circumcaval ureter, not included in the diagram are 1 child, 2 adults and 4 whose age was not stated. 4 of the patients in their second decade were under 12 years of age.

Fig. 4. Diagram to show the ureteric curvature as outlined by retrograde pyelography in Type I and Type II circumcaval ureter.

normal or showed only minimal dilatation (Table II). 7 of these 12 had been operated upon, though in 5 it seems possible that the operation was unnecessary in view of the lack of obstruction.

Operative Findings

There has at times been some doubt as to the cause of obstruction in the circumcaval ureter, it often seems in the Type I cases that the descending segment is dilated but the dilatation stops short at the psoas muscle where the ureter turns upwards, rather than at the point where it lies posterior to the vena cava (Bateson and Atkinson, 1969). Our case 1 (Fig. 1) demonstrates much greater dilatation in the descending than in the ascending limb of the lumbar ureter. In general it seems likely that venous compression is the primary cause and that ureteric kinks, either at the junction between the ascending and the descending limb or at the pelvi-ureteric junction produce a secondary obstruction. However the absence of obstruction in Type II cases, where there is a smooth curve away from the renal pelvis, suggests that kinks are the more important factor. Of the 134 Type I cases operated upon, there was no mention of the state of the retrocaval segment in 11; of the remainder this segment was stenosed in 28% but only compressed in 72%. The stricturing appears to be of late development, perhaps on the basis of longstanding ureteritis. In Young's case (1947) the retrocaval segment passed through a fibrous tunnel but was not strictured, while in Lich and Grant's case (1949) the ureter was compressed by a crotch formed by the vena cava and a vertebral tributary.

Contralatèral Anomalies

The circumcaval ureter was on the right side in all but 1 case. A left-sided example was reported by Brooks (1962) in a case of situs inversus. The left kidney was also abnormal in 12 cases, being agenetic in 6, ectopic in 2, hydronephrotic in 2, malrotated or hypoplastic in each of 2 further examples.

Table I

Presentation in 162 Cases with Circumcaval Ureter

Manifestation	Number		Percentage	
Renal pain	85	114	52·5	70·4
Renal colic	29		17·9	
Urinary infection	38		23·5	
Haematuria	35		21·6	
Others	20		12·3	

Cardiovascular Anomalies

Circumcaval ureter is usually regarded as the result of anomalous development of the inferior vena cava. It is, therefore, rather surprising to find that identifiable venous anomalies are rather uncommon. In Lindholm, Lantto and Svartholm's case (1972) it was demonstrated that bilateral venae cavae were present. In both Le Page and Baldwin's case (1972) and in that reported by Irikura, Minami and Machida (1973) it was shown that the ureter passed through a right vena caval ring. At operation bilateral venae cavae were also found by Nielsen (1959) and Harrill (1940) and by de Gironcoli (1962). Cardiac or arterial anomalies were found in 4 cases.

The Operation

The operations undertaken for circumcaval ureter as reported in the literature are set out in Table III. There has been considerable discussion as to the advisability of excising the retrocaval segment and authors have naturally been influenced by the particular findings in their own cases. In recent years, however, much greater experience has been gained of remodelling ureters involved in congenital obstructions, so that certain general rules can be laid down. Damaged and avascular segments must be excised, kinks must be straightened whenever this is possible without jeopardising the blood supply of the distal ureter; the pelvi-ureteric junction requires correction if secondarily obstructed; uretero-ureteric anastomosis must be long and oblique without any abrupt transition from the dilated to the narrow segment; the new junction should be splinted and the renal pelvis should be drained, if necessary by a T-tube passing through the anastomosis and emerging below it. Observance of these rules presents little difficulty in the case of circumcaval ureter and in childhood should produce excellent results provided renal damage is not already irreversible. Greater but not insuperable difficulties may be encountered later in life, but some of the reported failures were clearly due to infractions of these rules, as for instance when an end-to-end anastomosis of the ureter was made. The place for any other form of treatment must be small: division of the inferior vena cava may be sensible with a double cava or if a ring vessel is present, but division of the normal cava, although technically possible and safe, does nothing to improve the important secondary pathology in the ureter.

Summary

4 cases of circumcaval ureter presenting in childhood are reported.

A review of the literature reveals that most cases receive attention only later in life at a time when ureteric changes are not so readily reversible.

Table II

Analysis of the 12 Cases with Circumcaval Ureter Type 2

Author	Presentation	Pelvicalyceal radiology	Operation	Comment
Baker, 1955	Hypertension	Blunt calyces	Ureteral anastomosis	Operation unnecessary (and hypertension unchanged)
Bitker, 1965 (Case 2)	Recurrent cystitis	Normal	None	...
Brizon and Delaneau, 1961	Right renal colic	Normal	Pelviureteric anastomosis	Pain cured
Brule et al., 1962 (Case 2)	Right lumbar pain	Normal but lower calyceal stone	Ureteral anastomosis and nephrolithotomy	Operation on ureter unnecessary
Cendron and Reis, 1972 (Case 4)	Haematuria	Horseshoe kidney, some right dilatation and a calyceal stone	Ureteral anastomosis, pyelolithotomy and nephropexy	Had previous right pyelolithotomy. Operation on ureter unnecessary*
Chauvin, 1953	Right renal colic and prostatism (large prostatic adenoma)	Slight dilatation of renal pelvis	Nil on ureter	...
Chauvin, 1954 (Case 2)	Right loin pain	Some dilatation	Nil	...
Couvelaire and Richet, 1952	Right renal colic	Normal	Nil	...
Lange *et al.*, 1963	Mild right renal colic	Slight dilatation	Ureteral anastomosis	Pain cured
Presman and Firfer, 1956†	Hypertension	Blunt calyces	Ureteral anastomosis	Operation unnecessary
Qureshi and Mulvaney, 1965	Cystitis and recurrent abdominal pain	Normal but nephroptosis	Ureteral anastomosis and nephropexy	Operation on ureter unnecessary
Verriere, 1962	Prostatism (small adenoma)	Slight dilatation of renal pelvis	Resection of prostatic adenoma	...

* From author's operative note on the ureter it was the "same calibre before and after crossing the inferior vena cava".

† A replica of Baker's case (1955) but there is no mention of it being previously reported. From the author's operative note "the ureter was normal in appearance" and "the kidney appeared grossly normal with an intrarenal pelvis".

A study of the course of the ureter reveals that 2 forms can be distinguished: a common Type I with a low loop and kinking of the proximal ureter producing obstruction and a rare Type II with a high loop where there is no kinking and no obstruction.

Ureteric remodelling on the ordinary principles formulated for congenital obstructions can give good results.

Table III

Operative Procedures and Results in 109 Patients with Circumcaval Ureter

Operation	Number	Good	Unchanged	Secondary nephrectomy	No postoperative X-ray
Transverse ureteral anastomosis	40 } 66	21 } 41	9 } 13	3 } 3	7 } 9
Oblique ureteral anastomosis	26	20	4	...	2
Pyelopelvic anastomosis	21	16	4	...	1
Anderson-Hynes pyeloplasty	10	7	2	...	1
Pyeloureteric anastomosis	5	3	2	...	...
Others	7	3	1	...	3

References

Abeshouse, B. S. and Tankin, L. H. (1952). Retrocaval ureter; report of a case and a review of the literature. *American Journal of Surgery*, **84**, 383-393.

Aboulker, P. and Motz, C. (1953). Un cas d'uretère rétrocave. *Journal d'Urologie et de Néphrologie*, **59**, 391-392.

Anderson, J. C. and Hynes, W. (1949). Retrocaval ureter. A case diagnosed pre-operatively and treated successfully by a plastic operation. *British Journal of Urology*, **21**, 209-214.

Antopol, W. and Yelin, G. (1939). Postcaval ureter. *Urologic and Cutaneous Review*, **43**, 746-752.

Auvert, J. (1965). Discussion of paper of Rognon and Pillet. *Journal d'Urologie et de Néphrologie*, **71**, 943.

Auvray, P. (1967). Uretère rétrocave. *Acta Urologica Belgica*, **35**, 638-640.

Baker, W. J. (1955). Discussion of paper of Pratt and Newton. *Transactions of the Southeastern Section of the American Urological Association*, **19**, 23-26.

Bateson, E. M. and Atkinson, D. (1969). Circumcaval ureter: new classification. *Clinical Radiology*, **20**, 173-177.

Bauer, K. M. (1958). Die gefässbedingte Harnstauungsniere (Retrokavaler Ureter). *Beiträge zur klinischen Chirurgie*, **197**, 179-183.

Beard, D. E. and Goodyear, W. E. (1950). Retrocaval ureter; a case report. *Urologic and Cutaneous Review*, **54**, 80-82.

Berjian, R. A. (1967). Retrocaval ureter: report of a case with operative correction. *Journal of the American Osteopathic Association*, **66**, 621-626.

Bitker, M. P. (1965). Réflexions sur l'uretère rétrocave (sur 3 observations inédites et revue de la littérature). *Journal d'Urologie et de Néphrologie*, **71**, 851-865.

Blundon, K. E. (1962). The treatment of retrocaval ureter in the solitary kidney. *Journal of Urology*, **88**, 29-32.

Bohn, C. L. S. (1956). Retrocaval ureter. *Nordisk Medicin*, **55**, 651-653.

Brito, R. R., Zulian, R., Albuquerque, J. and Berges, H. J. (1973). Retrocaval ureter. *British Journal of Urology*, **45**, 144-152.

Brizon, J. and Delaneau, J. (1961). A propos d'un nouveau cas d'uretère rétrocave. *Journal d'Urologie et de Néphrologie*, **67**, 293-299.

Brooks, R. J. (1962). Left retrocaval ureter associated with situs invertus. *Journal of Urology*, **88**, 484-487.

Brule, A. E., Lacroix, A. and Koebele, F. (1962). Uretère rétrocave. *Journal d'Urologie et de Néphrologie*, **68**, 201-206.

Campbell, G. D. and Anderson, J. C. (1965). Retrocaval ureter. *Australian and New Zealand Journal of Surgery*, **35**, 41-51.

Campos Freire, G. (1953). Uretère rétrocave et rein hypoplasique. *Journal d'Urologie et de Néphrologie*, **59**, 868-872.

Cathro, A. J. (1952). Section of the inferior vena cava for retrocaval ureter: a new method of treatment. *Journal of Urology*, **67**, 464-475.

Cendron, J. and Reis, C. F. (1972). L'uretère rétrocave chez l'enfant. A propos de 4 cas. *Journal d'Urologie et de Néphrologie*, **78**, 375-392.

Chauvin, H. F. (1953). Uretère rétrocave probable décelé à l'urographie intraveineuse. *Journal d'Urologie et de Néphrologie*, **59**, 254-255.

—— (1954). Sur les images radiologiques d'uretère rétrocave. *Journal d'Urologie et de Néphrologie*, **60**, 266-269.

Considine, J. (1966). Retrocaval ureter. A review of the literature with a report on two new cases followed for 15 years and 2 years respectively. *British Journal of Urology*, **38**, 412-423.

Corbus, B. C. J. (1948). Retrocaval ureter. *Urologic and Cutaneous Review*, **52**, 535-536.

Couvelaire, R. (1953). Autre exemple d'uretère rétrocave. *Journal d'Urologie et de Néphrologie*, **59**, 65-66.

Couvelaire, R. and Richet, G. (1952). Un exemple d'uretère rétrocave. *Journal d'Urologie et de Néphrologie*, **58**, 384-385.

Creevy, C. D. (1948). Recognition and surgical correction of retrocaval ureter: a case report. *Journal of Urology*, **60**, 26-30.

Cukier, J., Aubert, J. and Dufour, B. (1969). Uretère rétrocave et rein en fer à cheval chez un garçon hypospade de 6 ans. *Journal d'Urologie et de Néphrologie*, **75**, 749-757.

De Gironcoli, F. (1962). Retrocaval ureter. Report of a case, review of the literature and observations on surgery. *Acta chirurgica Academiae Scientarium Hungaricae*, **3**, 137-152.

Délivéliotis, A. and Varkarakis, M. (1964). Trois cas d'uretère rétrocave. *Journal d'Urologie et de Néphrologie*, **70**, 365-370.

Dougherty, J. A. (1951). Circumcaval ureter. *California Medicine*, **75**, 48-50.

Dreyfuss, W. (1959). Anomaly simulating a retrocaval ureter. *Journal of Urology*, **82**, 630-632.

Ducassou, J., Martin-Laval, D., Richaud, C., Benady, F. and Picaud, R. (1964). Uretère rétrocave. *Journal d'Urologie et de Néphrologie*, **70**, 656-657.

Duff, P. A. (1950). Retrocaval ureter: case report. *Journal of Urology*, **63**, 496-499.

Dufour, A. (1963). L'uretère rétrocave. *Bulletin de l'Académie nationale de médecine*, **147**, 522-529.

Dufour, A. and Sesboüe, P. (1952). Uretère rétrocave diagnostique avant l'opération et guéri par uretéroplastie. *Journal d'Urologie et de Néphrologie*, **58**, 390-393.

Ekström, T. and Nilson, A. E. (1959). Retrocaval ureter. Two roentgenographically diagnosed and surgically corrected cases. *Acta chirurgica Scandinavica*, **118**, 53-59.

Fletcher, E. W. L. and Lecky, J. W. (1971). Retrocaval ureter obstructed by an aberrant renal artery. *Journal of Urology*, **106**, 184-185.

Gdanietz, Von K. (1966). Beitrag zum retrokavalen Ureter im Kindesalter. *Zeitschrift für Kinderchirurgie und Grenzgebiete*, **3**, 83-91.

Godde, Von S. (1972). Beitrag zur Klinik und Therapie des retrokavalen Harnleiters. *Zeitschrift für Urologie und Nephrologie*, **65**, 739-748.

Goodwin, W. E., Burke, D. E. and Muller, W. H. (1957). Retrocaval ureter. *Surgery, Gynecology and Obstetrics*, **104**, 337-345.

Goyanna, R., Cook, E. N. and Counseller, V. S. (1946). Circumcaval ureter: report of case in which diagnosis was made preoperatively. *Mayo Clinic Proceedings*, **21**, 356-360.

Greene, L. F. and Kearns, W. M. (1946). Circumcaval ureter: report of case with consideration of the pre-operative diagnosis and successful plastic repair. *Journal of Urology*, **55**, 52-59.

Gregersen, P. L. (1946). Ectopic course of the ureter attended with hydronephrosis. *Acta Chirurgica Scandinavica*, **93**, 552-562.

Grossman, S. L. and Fehr, J. U. (1953), Retrocaval ureter. *American Journal of Surgery*, **85**, 679-682.

Guillemin, P. (1958). Uretère rétrocave. *Revue Médicale de Nancy*. **83**, 575-578.

Hamm, F. C., Weinberg, S. R. and Waterhouse, R. K. (1962). End to end ureteral anastomosis: a simple original technique. *Journal of Urology*, **87**, 43-47.

Harrill, H. C. (1940). Retrocaval ureter: report of case with operative correction of the defect. *Journal of Urology*, **44**, 450-457.

Heslin, J. E. and Mamonas, C. (1951). Retrocaval ureter: report of 4 cases and review of the literature. *Journal of Urology*, **65**, 212-222.

Hesse, V. E. (1969). Retrocaval ureter. *South African Medical Journal*. **43**, 561-564.

Hradcova, L. and Kafka, V. (1963). Retrocaval ureter in childhood. *Urologia Internationalis*, **16**, 103-116.

Hughes, F. A., Barcia, A., Cortes, R. and Nogueira Graf, A. (1960). Considérations sur l'uretère rétrocave. A propos d'un nouveau cas. *Journal d'Urologie et de Néphrologie*, **66**, 299-310.

Hyams, B. B., Schneiderman, C. and Mayman, A. B. (1968). Retrocaval ureter. *Canadian Medical Association Journal*, **98**, 45-49.

Irikura, M., Minami, T. and Machida, T. (1973). A rare case of retrocaval ureter. *Japanese Journal of Urology*, **64**, 319-323.

Jacobson, C. E. (1950). Retrocaval ureter: case report. *Connecticut Medicine*, **14**, 709-713.

Johansson, N. T., Nilsson, S., Schersten, T., Schwartz, J. and Weiland, P. O. (1969). Retrocaval ureter. Report of a case and short review of literature. *Scandinavian Journal of Urology and Nephrology*, **3**, 53-58.

Keweloh, Von E. and Schmitz, W. (1970). Zur operativen Behandlung des retrokavalen Ureters. *Zentralblatt für Chirurgie*, **95**, 420-423.

Kimbrough, J. C. (1935). Surgical treatment of hydronephrosis. *Journal of Urology*, **33**, 97-109.

Kottász, S. and Magasi, P. (1973). Über die chirurgische Losung des retrokavalen Ureters mit Nierenstein. *Acta chirurgica Academiae Scientarium Hungaricae*, **14**, 53-58.

Laidig, C. E. and Pierce, J. M. (1959). Retrocaval ureter, unusual cause of ureteral obstruction. *Journal of the American Medical Association*, **171**, 2312-2314.

Lange, J. (1956). Uretère rétrocave diagnostic radiologique préopératoire; décroisement. *Journal d'Urologie et de Néphrologie*, **62**, 472-475.

Lange, J., Bonnemaison, J., Etcheverry, M. and Lange, D. (1963). Un second cas personnel d'uretère rétrocave opéré. *Journal d'Urologie et de Néphrologie*, **69**, 721-724.

Laughlin, V. C. (1954). Retrocaval (circumcaval) ureter associated with solitary kidney. *Journal of Urology*, **71**, 195-199.

Leberman, P. R., Zinsser, H. H. and Franklin, M. (1952). Retrocaval ureter; case report and a new diagnostic approach. *Journal of Urology*, **68**, 679-683.

Lemaitre, G., Toison, G., Defrance, G. and Mazeman, E. (1963). Deux observations d'uretère rétrocave. *Journal de Radiologie, d'Electrologie et de Médecine Nucléaire*, **44**, 332-334.

Le Page, J. R. and Baldwin, G. N. (1972). Obstructive periureteric venous ring. *Radiology*, **104**, 313-315.

Lerman, I., Lerman, S. and Lerman, F. (1956). Retrocaval ureter: report of a case. *Journal of the Medical Society of New Jersey*, **53**, 74-77.

Lich, R. and Grant, O. (1949). Retrocaval ureter. *Archives of Surgery*, **59**, 84-91.

Lindholm, A., Lantto, S. and Svartholm, F. (1972). Retrocaval ureter: report of a case. *Scandinavian Journal of Urology and Nephrology*, **6**, 203-205.

Löfgren, L. and Heikkinen, E. (1966). Retrocaval ureter. *Annales Chirurgiae et Gynaecologiae Fenniae*, **55**, 46-52.

Lowsley, O. S. (1946). Postcaval ureter with description of a new operation for its correction. *Surgery, Gynecology and Obstetrics*, **82**, 549-556.

Lyter, C. S. and Meyer, W. C. (1949). Retrocaval ureter: case report. *Urologic and Cutaneous Review*, **53**, 718-720.

Maquinay, C. and Pirlet, F. (1959). Un cas d'uretère rétrocave. Traitement chirurgical conservateur. Résultat de cinq ans. *Acta Urologica Belgica*, **27**, 133-138.

Marcel, J. E. (1953). Grosse hydronephrose par uretère rétrocave. *Archives Françaises de Pédiatrie*, **10**, 274-282.

May, F. (1938). Verstopfungsniere bei dorsalem Ureterverlauf. *Zeitschrift für Urologie und Néphrologie*, **32**, 316-320.

Mayer, R. F and Mathes, G. L. (1958). Retrocaval ureter. *Southern Medical Journal*, **57**, 945-950.

McCrea, A. N. (1958). Retrocaval ureter replaced by a segment of ileum. *British Journal of Urology*, **30**, 315-318.

McElhinney, P. P. B. and Dorsey, J. W. (1948). Retrocaval ureter: case report. *Journal of Urology*, **59**, 497-500.

Mestdag, G., Auvray, P. and Piront, A. (1971). Uretère rétrocave et rein unique congénital. *Acta Urologica Belgica*, **39**, 517-521.

Middleton, A. W. (1951). Postcaval ureter; a case preoperatively diagnosed with confirmation at surgery. *Rocky Mountain Medical Journal*, **48**, 186-190.

Molina, L. F. R. and Sabucedo, R. M. (1957). Ureter retrocaval. *Radiologia*, **7**, 115-119.

Motz, C. (1962). Discussion of paper by Vittori et al. *Journal d'Urologie et de Néphrologie*, **68**, 443.

Mullen, W. E. and Engel, W. J. (1952). Circumcaval ureter. *Radiology*, **59**, 528-537.

Neveu, J. (1959). Deux cas d'uretère rétrocave. *Semaine des Hôpitaux de Paris*, **35**, 876-877.

Nielsen, B. P. (1959). Retrocaval ureter: report of a case. *Acta radiologica*, **51**, 179-188.

Nourse, M. H. and Moody, H. C. (1946). Postcaval ureter: report of a surgical case. *Journal of Urology*, **56**, 525-529.

Olmer, M., Richaud, C., Salvadori, J. M., Kasbarian, M., Bouvenot, G. and Ducros, J. (1971). L'uretère rétrocave (à propos d'une observation). *Marseille-médical*, **108**, 861-864.

Olson, R. O. and Austen, G. (1950). Postcaval ureter. Report and discussion of a case with successful surgical repair. *New England Journal of Medicine*, **242**, 963-968.

Oshin, D. R. (1964). Retrocaval ureter: an unusual complication associated with pregnancy. *Journal of Urology*, **91**, 652-653.

Parks, R. E. and Chase, W. F. (1951). Retrocaval ureter: report of 2 cases diagnosed preoperatively in childhood. *American Journal of Diseases of Children*, **82**, 442-445.

Peisojovich, M. R. and Lutz, S. J. (1969). Retrocaval ureter: a case report and successful repair with a new surgical technique. *Michigan Medicine*, **68**, 1137-1141.

Pick, J. W. and Anson, B. (1940). Retrocaval ureter: report of a case with a discussion of its clinical significance. *Journal of Urology*, **43**, 672-685.

Pitt, D. C. (1965). Retrocaval ureter: report of a case diagnosed preoperatively by intravenous and retrograde pyelography. *Radiology*, **84**, 699-702.

Pratt, A. M. and Newton, R. G. (1955). Retrocaval ureter: a report of 2 cases and review of the literature. *Transactions of the South-eastern Section of the American Urological Association*, **19**, 18-26.

Presman, D. and Firfer, R. (1956). A diagnostic method for retrocaval ureter. *American Journal of Surgery*, **92**, 628-631.

Qureshi, M. A. and Mulvaney, W. P. (1965). Retrocaval ureter: report of two cases. *American Surgeon*, **31**, 50-52.

Randall, A. and Campbell, E. W. (1935). Anomalous relationship of the right ureter to the vena cava. *Journal of Urology*, **34**, 565-583.

Revol, G. (1966). Un cas d'uretère rétrocave avec lithiase. *Journal d'Urologie et de Néphrologie*, **72**, 749-752.

Rognon, L. M. and Pillet, J. (1965). La cavographie dans le diagnostic préopératoire de l'uretère rétrocave. *Journal d'Urologie et de Néphrologie*, **71**, 936-942.

Rowland, H. S., Bunts, R. C. and Iwano, J. H. (1960). Operative correction of retrocaval ureter: a report of four cases and review of the literature. *Journal of Urology*, **83**, 820-833.

Sabatini, S. A. and Wessler, G. (1950). Retrocaval ureter: case report. *Urologic and Cutaneous Review*, **54**, 720-721.

Sapsin, S. S. and Jacobsen, M. E. (1951). Retrocaval ureter. *Texas Journal of Medicine*, **47**, 716-717.

Schmidt, C. R., Huebert, D. W. and Beazell, J. M. (1951). Retrocaval ureter. *Archives of Surgery*, **62**, 299-302.

Schwartz, J. W. and Irey, N. S. (1949). Postcaval ureter: report of a case. *Urologic and Cutaneous Review*, **53**, 327-329.

Servantie, G. (1956). Un Cas d'uretère rétrocave. *Journal de Radiologie, d'Electrologie et de Médecine Nucléaire*, **37**, 935-937.

Shearer, T. P. (1949). Retrocaval ureter: report of a case with successful plastic repair. *Journal of Urology*, **63**, 152-157.

Shih, H. E. (1937). Postcaval ureter. *Journal of Urology*, **38**, 61-66

Shown, T. E. and Moore, C. A. (1971). Retrocaval ureter: 4 cases. *Journal of Urology*, **105**, 497-501.

Stoll, Von E. and Ruza, J. (1965). Retrocaval verlaufender rechter Ureter bei einem elfjährigen Kind und seine operative Korrektur. *Helvetica Paediatrica Acta*,, **20**, 456-465

Truc, E., Mirouze, J., Levallois, M., Henriet, R., Pons, J. C. and Acconcia, G. (1959). Une observation d'uretère rétrocave (diagnostic préopératoire par la cavographie, confirmation par l'intervention). *Journal d'Urologie et de Néphrologie*, **65**, 941-944.

Uebelhör, R. (1936). Hydronephrose bei Abnormität der unteren Hohlevene. *Zeitschrift für Urologie und Nephrologie*, **30**, 769-772

Uson, A. C., Braham, S. B., Abrams, C. A. L. and Berdon, W. E. (1970). Retrocaval ureter in a child with Turner's syndrome. *American Journal of Diseases of Children*, **119**, 267-269.

Van Regemorter, G. (1969). L'uretère rétrocave. *Acta Urologica Belgica*, **37**, 450-452.

Van Tassel, C. (1953). Retrocaval ureter. *United States Armed Forces Medical Journal*, **4**, 1486-1490.

Van Velzer, D. A., Barrick, C. W. and Jenkinson, E. L. (1955). Postcaval ureter. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine*, **74**, 490-492.

Verrière, P. (1962). Un cas d'uretère rétrocave. *Journal d'Urologie et de Néphrologie*, **68**, 712-715.

Vittori, J., Maine, D. and Quinard, J. (1962). Un cas d'uretère rétrocave. *Journal d'Urologie et de Néphrologie*, **68**, 440-443.

Voelkel, H. H. (1963). Retrokavaler Verlauf des rechten Ureters. *Zeitschrift für Urologie und Nephrologie*, **56**, 49-60.

Wang, Yi-Ching, Chiang, Y., Wu, C. and Wang, C. (1963). Retrocaval ureter. *China Medical Journal*, **82**, 538-540.

Williams, L. R. and Ankenman, G. J. (1957). Circumcaval ureter. *Canadian Medical Association Journal*, **76**, 744-747.

Wilson, C. L. and Herzlich, J. (1944). Postcaval ureter. *Journal of Urology*, **51**, 14-18.

Young, J. N. (1947). Retrocaval ureter with description of an operation in a case complicated by ureteric calculus. *British Journal of Urology*, **19**, 22-28.

Younger, E. Chacon, V., Anllo and Oroza. (1960). Deux cas d'uretère rétrocave. Traitement conservateur. Anastomose urétéro-urétérale précave. *Journal d'Urologie et de Néphrologie*, **66**, 385-393.

The Authors

M. M. Kenawi, MCh, DS, FRCSE, FRCS. Surgeon, Faculty of Medicine, Cairo University.
D. Innes Williams, MD, MCh, FRCS, Consultant Surgeon.

British Journal of Urology (1976), **48**, 193-198 ©

Abnormalities of Detrusor and Sphincter Function in Multiple Sclerosis

JENS T. ANDERSEN and WILLIAM E. BRADLEY
Department of Neurology, University of Minnesota, Minneapolis, Minnesota

The occurrence and incidence of neurogenic bladder dysfunction in multiple sclerosis have been documented in clinical studies (Poskanzer, Schapers and Miller, 1963; Miller, Simpson and Yeates, 1965). However, only a few studies have focused on the specific disturbances of the micturition reflex and sphincter function in this disease (Bradley, Logothetis and Timm, 1973; Hebjørn, 1973). 52 patients, 38 women and 14 men with multiple sclerosis were investigated using gas-cystometry and spincter electromyography. We found that disturbances of detrusor and urethral function with subsequent incontinence represented by far the largest clinical problem, whereas no signs of upper urinary tract involvement was documented.

Patients and Methods

The mean age of the 62 patients investigated was 41·9 years (range: 22 to 73 years) and the mean duration of multiple sclerosis was 12·2 years with a range of 1 to 36 years. Urinary bladder symptoms were present in 49 of the patients and the mean duration of the voiding symptoms was 4·9 years (range: 1 to 24 years). The main symptoms are shown in Figure 1. Urgency of micturition was the predominant complaint (71·2 % of the patients) followed by urge-incontinence which was present in 50 % of the patients.

Urgency was defined as loss of ability voluntarily to suppress the sensation of a strong desire to void. Urge-incontinence was found in 57·9 % of the female patients but only in 28·6 % of the male patients. This difference is statistically significant ($P < 0{\cdot}01$) and confirms the findings of Bradley *et al.* (1973).

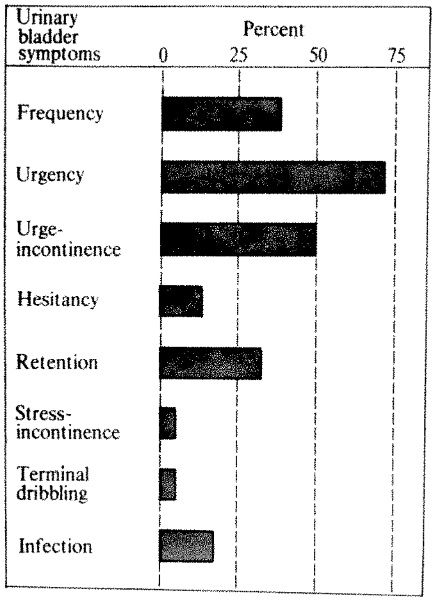
Frequency of voiding above the usual schedule of the patients was found in 38·5 % whereas 32·7 % complained of urinary retention. Infection was found in 9 patients (17·3 %), 8 females and 1 male.

Detrusor Function. Was assessed by means of gas-cystometry (Bradley, Timm and Scott, 1975).

The patients were catheterised with an indwelling urethral catheter and cystometry was performed using CO_2 as filling medium at a constant inflation rate of 200 ml per minute. The investigation was done with the patients in supine, sitting, standing and walking-in-place positions. Intravesical pressure was recorded with a transducer amplifier calibrated in centimetres of water and connected to a two-channel strip chart recorder. The interpretation of the cystometrogram (CMG) was based on the following parameters: presence and threshold of the detrusor reflex, the patients' ability voluntarily to suppress the reflex and the volume-pressure relations referred to as the tonus limb of the CMG (Ruch, 1960). The use of gas-cystometry has several advantages compared with the traditional water cystometry. The low viscous drag artifact permits flow rates up to 300 ml per minute. This may be utilised to shorten the test time and permits repetitive testing in different postural positions. The rapid filling may also be used to detect detrusor instability.

Sphincter Function. Was studied recording anal sphincter activity utilising electronic integration (Bradley *et al.*, 1967). By simultaneous recording of the electromyographic activity in the peri-urethral striated sphincter and the anal sphincter we found that anal sphincter activity reflects the concurrent activity in the striated urethral sphincter during detrusor contraction. A bipolar

①



②

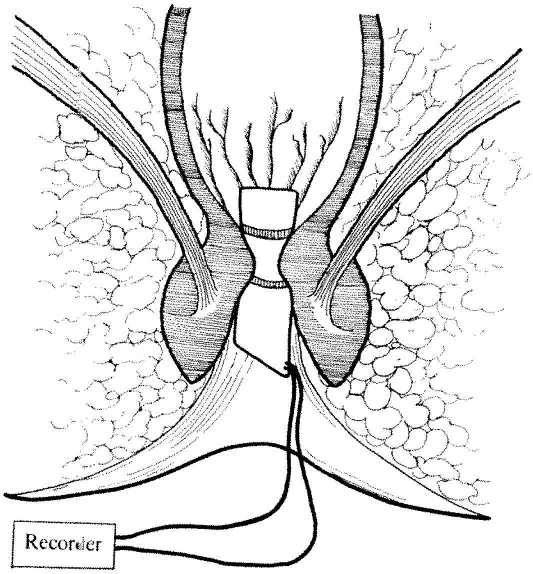


Fig. 1. Distribution of the main urinary symptoms in 52 patients with multiple sclerosis.

Fig. 2. Anal plug with concentric electrodes for recording of the electromyographic activity of the anal sphincter.

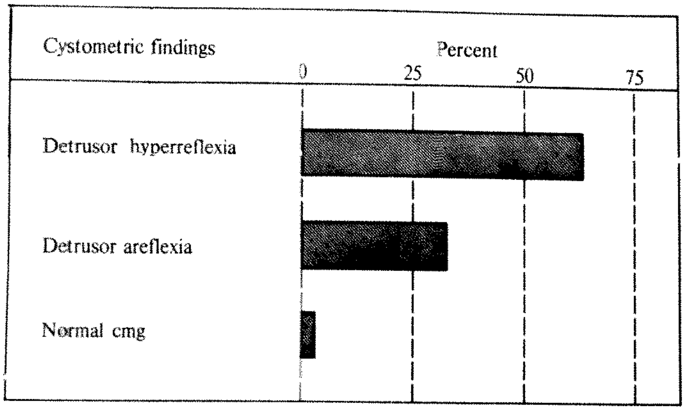


Fig. 3. Cystometric findings in 52 patients with multiple sclerosis.

concentric EMG recording electrode mounted on a teflon, hour-glass-shaped anal plug was inserted in the anal canal (Fig. 2). Electromyographic activity was recorded simultaneously with the CMG on the second channel of the strip chart recorder. The EMG-potentials were integrated and recorded in arbitrary units. The voluntary control of the sphincter-mechanisms was tested asking the patients to contract and relax the anal sphincter.

Presence of urinary infection was judged by urine culture using quantitative bacterial counts. Urinary infection was defined by the finding of more than 100,000 bacterial colonies per ml urine.

Involvement of the upper urinary tract was assessed by intravenous pyelography and the values of Blood Urea Nitrogen and Serum-Creatinine.

④

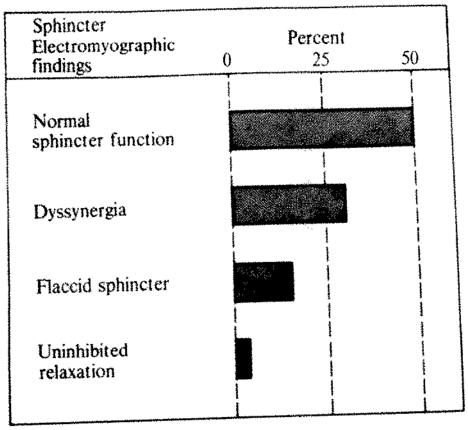


Fig. 4. Results of sphincter electromyography in 52 patients with multiple sclerosis.

⑤

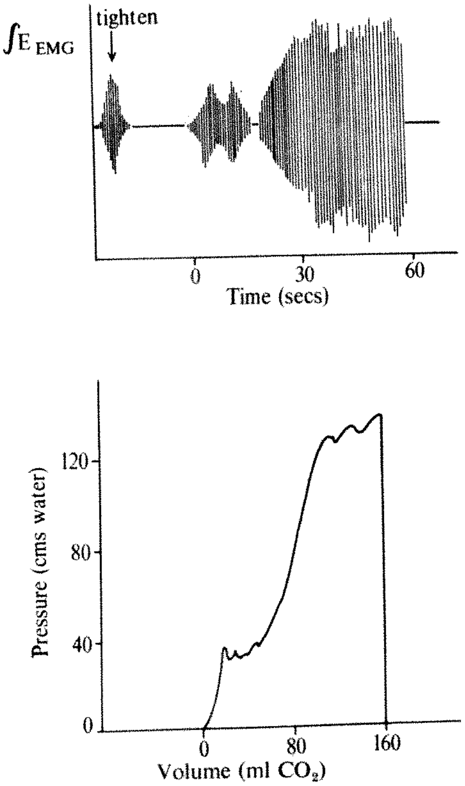


Fig. 5. Cystometric and sphincter-EMG recording showing detrusor hyperreflexia and sphincter dyssynergia from a 26-year-old female with a 1-year history of multiple sclerosis.

Cystometric Findings

The cystometric results are seen in Figure 3. Two types of detrusor reflex abnormalities were discovered: (1) Detrusor hyperreflexia, which was present in 63·5% of the patients; (2) Detrusor areflexia—seen in 32·7% of the patients. Finally, 3·8% showed a normal CMG.

Detrusor Hyperreflexia. Was defined by a CMG showing a detrusor reflex elicited at a low volume threshold (usually less than 150 ml) and the reflex could not be attenuated or inhibited voluntarily by the patient. The symptomatology in detrusor hyperreflexia consisted of urgency and frequency. Most of the female patients, furthermore, suffered from urge-incontinence.

Detrusor Areflexia. Was defined by a CMG showing absence of detrusor reflex even when the bladder was distended to the point of sensory discomfort. The majority of the patients with areflexia complained of difficulties in initiating micturition, straining and urinary retention. The duration of multiple sclerosis and voiding symptoms was not significantly longer in the patients with detrusor areflexia than in the remaining patients.

Testing for denervation supersensitivity according to the methods decsribed by Lapides *et al.* (1962) and Glahn (1970) was performed in 9 of the patients with detrusor areflexia. The response to Urecholine was positive in 5 of these patients but negative in the remaining 4 patients.

Sphincter Electromyography

26 of the patients (50%) showed a normal sphincter-EMG pattern implying full voluntary ability to contract and relax the anal sphincter on command. 3 pathological sphincter-EMG patterns were found (Fig. 4.)

Table

Combined Cystometric and Sphincter EMG-patterns in 52 Patients with Multiple Sclerosis

Detrusor function	Sphincter control	No. of patients
Normal	Normal	2
Hyperreflexia	Normal	15
Hyperreflexia	Dyssynergia	15
Hyperreflexia	Flaccid	1
Hyperreflexia	Uninhibited relaxation	2
Areflexia	Normal	9
Areflexia	Dyssynergia	1
Areflexia	Flaccid	7

1. **Sphincter Dyssynergia**. Characterised by increasing clonic sphincter activity on bladder filling. This activity could not be voluntarily suppressed by the patient. This abnormality—also referred to as uninhibited sphincter contraction—was found in 30·8% of the patients.

2. **Sphincter Paralysis** (flaccid sphincter). Implied absence of the ability to contract the sphincter on command. This condition was found in 8 patients (15·4%).

3. **Uninhibited Sphincter Relaxation.** Consisted of uncontrollable sphincter relaxation and was found in only 3·8% of our patients. This sphincter abnormality was associated with detrusor hyperreflexia in our cases but has also been reported combined with areflexia in multiple sclerosis (Bradley *et al.*, 1973).

Combined Cystometric and Sphincter Electromyographic Findings

The described abnormalities in detrusor and sphincter function were found in various combinations (Table). Detrusor hyperreflexia was most frequently combined with either normal sphincter control or sphincter dyssynergia. A typical recording of the latter pattern is shown in Figure 5. Areflexia was predominantly associated with either normal sphincter control or sphincter paralysis. In patients with detrusor areflexia and sphincter paralysis (Fig. 6) no sensation of bladder fullness was present and constant dribbling incontinence was present.

Upper urinary tract involvement was not found in any of our patients judged by intravenous pyelography and the values of B. U. N. and serum-creatinine.

Discussion

The present study shows a high incidence of disturbances of bladder function in multiple sclerosis. The distribution of bladder symptoms is in accordance with the findings of Miller *et al.* (1965) and the cystometric findings confirm the results of Hebjørn (1973) and Bradley *et al.* (1973). However, the simultaneous recording of the cystometrogram and the sphincter electrometrogram permits an easy and rapid evaluation of 2 important factors involved in micturition: detrusor reflex function and sphincter function.

Volitional control of the detrusor reflex is based on impulses from the cortical micturition centre governing the pontine-mesencephalic reticular formation. From here impulses in the reticulo-spinal tract influence the spinal micturition centre in the sacral grey matter. Interruption of these pathways results in a lowered threshold for the release of the detrusor reflex = detrusor

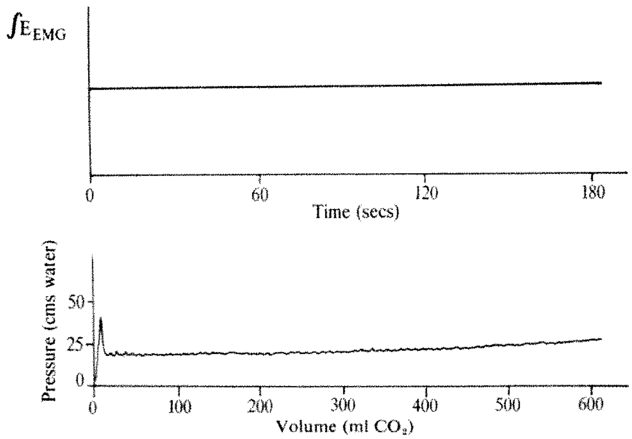


Fig. 6. Cystometric and sphincter-EMG recording showing detrusor areflexia and sphincter paralysis from a 22-year-old female with a 5 year history of multiple sclerosis.

hyperreflexia. Previous studies (Nathan and Smith, 1958) have documented, that the spinal pathways of the detrusor innervation are located in the lateral columns of the spinal cord. Furthermore, it has been reported (Fog, 1950) that the demyelinating plaques in the spinal cord in multiple sclerosis are mainly localised to the reticulo-spinal and pyramidal tracts. Thus it may be anticipated that clinical signs of pyramidal tract involvement are indicative of neurogenic bladder dysfunction in multiple sclerosis due to concurrent impairment of the reticulo-spinal tract. This is clinically documented by the high incidence of detrusor hyperreflexia in the present study, where, furthermore, 85% of the patients showed bilateral extensor plantar responses indicating a lesion of the pyramidal tract.

Normal sphincter function provides intact supraspinal control of the pudendal motor nucleus in the sacral grey matter. 50% of our patients showed impairment of the sphincter control giving rise to either dyssynergia, paralysis or uninhibited relaxation, indicating lesions located to the cortical-pudendal nucleus pathway.

The incidence of upper urinary tract involvement in multiple sclerosis has been reported varying from 21% (Damanski and Sutcliffe-Kerr, 1964) to 55% (Samellas and Rubin, 1965). Our material showed no evidence of back pressure effects. However, the reported series consisted of patients with far advanced disease and a significant longer duration of multiple sclerosis, than the patients in our study.

In conclusion, the present study has proved the need for detailed evaluation of the bladder and urethral function in patients with multiple sclerosis, since lower urinary tract dysfunction seems to represent the major clinical problem in the early phases of the disease.[1]

Summary

Bladder and urethral function was studied in 52 patients with multiple sclerosis using gas-cystometry combined with sphincter electromyography.

96% of the patients showed abnormalities of either detrusor or sphincter function.

The abnormal patterns discovered indicated demyelinating lesions in the corticospinal as well as in the reticulospinal tract.

---

[1] "Methods, definitions and units" conform to the standards proposed by the International Continence Society.

Urgency and urge-incontinence were the predominant symptoms, whereas no signs of involvement of the upper urinary tract was found.

The use of gas-cystometry provides a fast and differentiated method for assessment of the detrusor function.

References

BRADLEY, W. E., GLOVER, G., CONWAY, C. and MCCORMICK, S. (1967). Discriminator and integrator instrument for an on-line frequency analysis of single unit discharges. *Electroencephalography and Clinical Neurophysiology*, **22**, 177-179.

BRADLEY, W. E., LOGOTHETIS, J. L. and TIMM, G. W. (1973). Cystometric and sphincter abnormalities in multiple sclerosis. *Neurology*, **23**, 1131-1139.

BRADLEY, W. E., TIMM, G. W. and SCOTT, F. B. (1975). Cystometry I. *Urology*, **5**, 424-427.

DAMANSKI, M. and SUTCLIFFE-KERR, A. (1964). Paraplegia of non-traumatic origin and disseminated (multiple) sclerosis: urinary complications, their nature and treatment. *Acta Neurologica Psychiatrica Belgica*, **64**, 495-519.

FOG, T. (1950). Topographic distribution of plaques in the spinal cord in multiple sclerosis. *Archives of Neurology and Psychiatry*, **63**, 382-414.

GLAHN, B. E. (1970). Neurogenic bladder diagnosed pharmacologically on the basis of denervation supersensitivity. *Scandinavian Journal of Urology and Nephrology*, **4**, 13-24.

HEBJØRN, S. (1973), Neurogenic dysfunction of the bladder in disseminated sclerosis. A retrospective material. *Ugeskrift for Laeger*, **135**, 2317-2321.

LAPIDES, J., FRIEND, C. R., AJEMIAN, E. P. and REUS, W. S. (1962). Denervation supersensitivity as a test for neurogenic bladder. *Surgery, Gynecology and Obstetrics*, **114**, 241-244.

MILLER, H., SIMPSON, C. A. and YEATES, W. K. (1965). Bladder dysfunction in multiple sclerosis. *British Medical Journal*, **1**, 1265-1269.

NATHAN, P. W. and SMITH, M. C. (1958). The centrifugal pathway for micturition within the spinal cord. *Journal of Neurology, Neurosurgery and Psychiatry*, **21**, 177-189.

POSKANZER, D. C., SCHAPERS, K. and MILLER, H. (1963). Epidemiology of multiple sclerosis in the counties of Northumberland and Durham, *Journal of Neurology, Neurosurgery and Psychiatry*, **26**, 368-376.

RUCH, T. C. (1960). Central control of the bladder. In *Handbook of Physiology*, Section 1: *Neurophysiology*. Vol. 2. Washington, American Physiological Society, pp. 1270-1223.

SAMELLAS, W. and RUBIN, B. (1965). Management of upper urinary tract complications in multiple sclerosis by means of diversion to an ileal conduit. *Journal of Urology*, **93**, 548-552.

The Authors

Jens T. Andersen, MD, Assistant Professor.
William E. Bradley, MD, Professor.

British Journal of Urology (1976), **48**, 199-202 ©

A Case of Behçet's Disease involving the Bladder

G. F. CARSWELL
Urological Unit, Western General Hospital, Edinburgh

The co-existence of mouth and genital ulceration with iritis was first defined as a syndrome by Behçet (1937). It is now known to be a chronic and relapsing systemic disease, which involves many other systems. A review of the literature reveals rare renal involvement (Nestor *et al.*, 1970) but no previous account of bladder involvement has been found. A case of Behçet's disease involving the bladder is described below.

Discussion

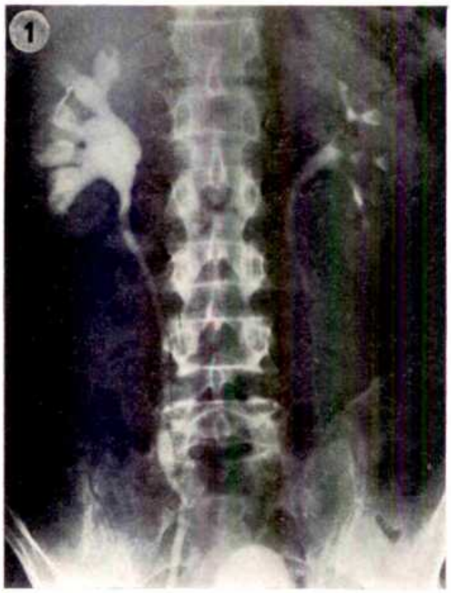
Behçet, a Turkish dermatologist, described the association of aphthous stomatitis, genital ulceration and recurrent iritis in 1937 but earlier accounts exist, the earliest being by Hippocrates (Feigenbaum, 1956).

The involvement of other organs is now well recognised. Lesions within the pharynx (Turner, 1972), oesophagus (Brodie and Ochsner, 1973), small bowel (Oshima *et al.*, 1963), central nervous system (Fowler *et al.*, 1968) and kidneys (Nestor *et al.*, 1970) have all been described. All 3 of Nestor's cases presented with the nephrotic syndrome. The histological findings revealed both extensive amyloid deposits in the glomeruli, the arterioles and the small arteries of the kidney and thrombophlebitis of the renal veins.

The unifying underlying pathological process affecting such a wide range of organs is a vasculitis, which may progress either to an occluding phlebitis or to a necrotising arteritis, with or without aneurysmal dilatation with thrombotic occlusion. Vascular occlusion is certainly a prominent feature of the disease. Deep venous thrombosis with recurrent pulmonary emboli (Cunliffe and Menon, 1969), superior vena caval and subclavian vein thrombosis (Decroix, 1969; Chajek and Fainaru, 1973) and arterial occlusion of the medium-sized arteries of the lower limb (Enoch, 1969; Mowat and Hothersall, 1969) have all been documented. The involvement of larger arterial vessels with the acute inflammatory reaction has led to aneurysmal dilatation of the aorta (Hills, 1967), the ulnar artery (Oshima *et al.*, 1963), the popliteal artery (Enoch, 1969) and the lobar pulmonary arteries (Davies, 1973).

The aetiology of Behçet's disease remains unresolved. Behçet first suggested a viral hypothesis, based on the finding of inclusion bodies in the cells of scrapings taken from mouth ulcers. Later, Sezer (1956) and Evans, Pallis and Spillane (1957) both claimed to have isolated and grown a virus from patients suffering from Behçet's disease but Dudgeon in a review in 1961, felt the evidence remained inconclusive.

Many authors now suggest that this disease is a systemic disorder belonging to the primary inflammatory connective tissue group of collagen diseases. There is certainly a high incidence of skin, joint and vascular manifestations in Behçet's disease which bears resemblance to such disorders as systemic lupus erythematosus, polyarteritis nodosa or temporal arteritis. It is on this hypothesis that treatment with high steroid dosage has been tried with varying success (Fowler *et al.*, 1968; Abdalla and Bahgat, 1973). The thrombotic episodes which so commonly occur, have been treated successfully by Cunliffe and Menon (1969) using the fibrinolytic drugs phenformin and ethyloestrenol and by Chajek and Fainaru (1973), using streptokinase. The latter authors demonstrated an increase in fibrinogen and Factor VIII levels associated with a decrease in fibrinolytic activity.



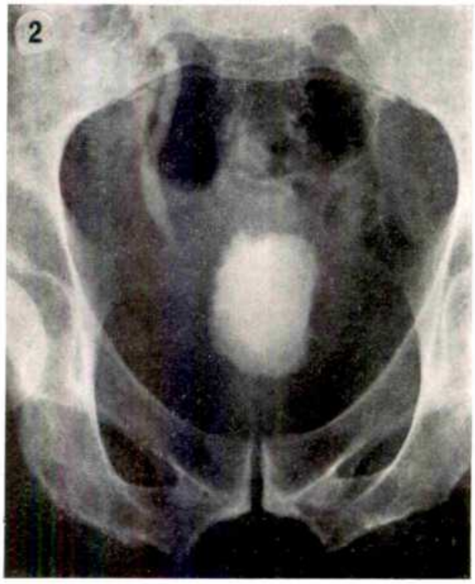


Fig. 1. Intravenous pyelogram showing partial right ureteric obstruction.

Fig. 2. Bladder contraction - partial right ureteric obstruction.

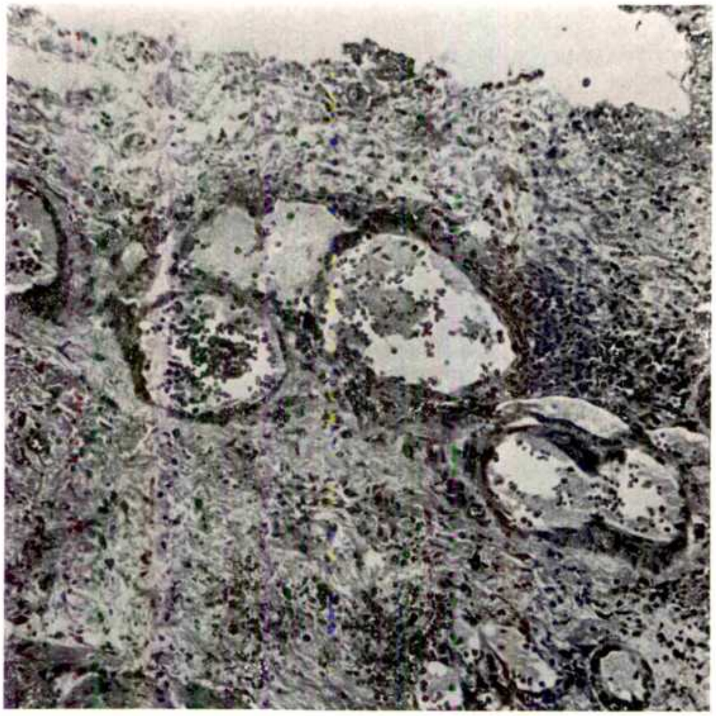


Fig. 3. Showing deep vessels in the bladder containing organising thrombus. (Magnification approximately × 500).

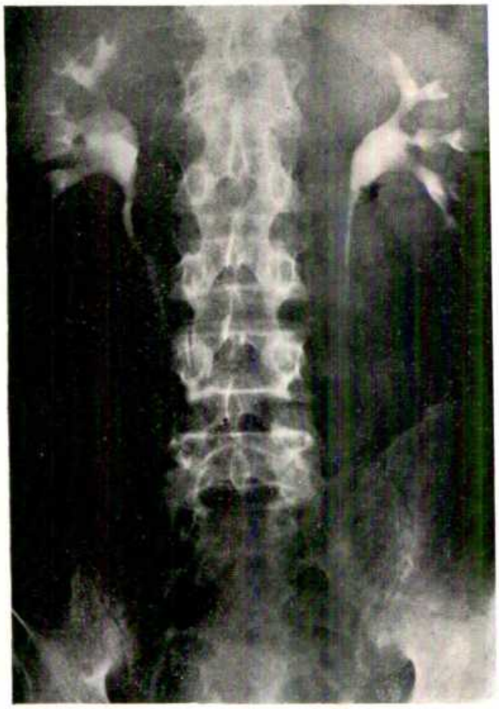


Fig. 4. Normal pyelogram 4 months later.

An autoimmune mechanism is now also thought to play a part in the development of the characteristic clinical picture of Behçet's disease.

Oshima *et al.*, (1963) demonstrated the presence of antibodies in the sera of patients against oral mucous membrane, using a tanned cell agglutination test, in 42% of cases. Similarly Lehner (1967) demonstrated antibodies against foetal oral mucous membrane using both haemagglutination and complement fixation tests, in approximately 80% of cases. Finally Morgenstern and Shearn (1973) reported a case of Behçet's disease with thymic hyperplasia, the changes being similar to those found in myasthenia gravis or Hashimoto's thyroiditis, known autoimmune diseases. It was on this autoimmune hypothesis that Abdalla and Bahgat (1973) carried out a controlled trial using the immunosuppressive agent, chlorambucil. They found that chlorambucil in conjunction with steroids was more successful than steroids alone in producing long-term remission of symptoms.

Case Report

A male aged 51, had suffered from Behçet's disease since the age 16. He had the classical triad of symptoms, plus arthralgia and chronic leg ulcers. A previous episode of gangrene of the right foot had eventually necessitated right forefoot amputation.

He was transferred from the Rheumatic Diseases Unit of the Northern General Hospital to the Urological Unit, Western General Hospital, Edinburgh, in August 1971, with a 4-day history of profuse haematuria with clotting and slight suprapubic pain.

No abnormality was detected in his genitourinary tract on physical examination. Healed pyodermal lesions on his trunk, chronic leg ulcers, a right symphathectomy scar and amputation of his right forefoot were the only positive findings.

Investigations

The haemoglobin level was 11·9 g per 100 ml, ESR was 98 mm in the 1st hour and the WBC count was 18,700, 87% being neutrophils. The blood urea and electrolyte estimations were within the normal range. The urine was sterile on culture. Intravenous urography revealed a moderate hydronephrosis and hydroureter on the right side (Fig. 1) and some bladder contraction (Fig. 2). At cystoscopy the bladder capacity was 250 ml. On the right lateral wall, involving the ureteric orifice and extending across the base on to the left wall were proliferative changes, which looked like necrotic anaplastic carcinoma. On bimanual examination the lesion was palpable on the right side of the bladder. The histology of the biopsy specimen showed acute inflammation with marked ulceration of the mucosa, but no evidence of tumour (Fig. 3). Because of this unexpected negative finding, cystoscopy and biopsy were repeated 2 days later. The final histological report again stated that no tumour was present in either biopsy specimen. The bladder wall was severely inflamed. A substantial portion of the mucosa had undergone necrosis and was infiltrated by fibrin and acute inflammatory cells. No primary vasculitis was seen in the submitted biopsy specimens, but the blood vessels seen in the sections examined were surrounded by an inflammatory exudate and several of them contained recent thrombi. It was concluded that thrombotic occlusion of small vessels had contributed to the necrosis of the bladder mucosa in this case of Behçet's disease.

The haematuria ceased 1 week after admission and did not recur. Intravenous urography 4 months after discharge showed a return to normal function on the right side (Fig. 4).

Summary

A case of Behçet's disease involving the bladder has been described. It resembled a bladder carcinoma.

The pathology, aetiology and treatment have been briefly outlined.

I am grateful to Mr W. Selby Tulloch and Mr J. E. Newsam for their permission to publish this case and to Dr Neil MacLean for his help with the pathology.

References

ABDALLA, M. I. and BAHGAT, N. E. (1973). Long-lasting remission of Behçet's disease after chlorambucil therapy. *British Journal of Ophthalmology*, **57**, 706-711.

BEHÇET, H. (1937). Über rezidivierende, aphthöse, durch ein Virus verursachte, Geschwüre am Mund, am Auge und an den Genitalien. *Dermatologische Wochenschrift*, **105**, 1152-1157.

BRODIE, T. E. and OCHSNER, J. L. (1973). Behçet's syndrome with ulcerative oesophagitis: report of the first case. *Thorax*, **28**, 637-640.

CHAJEK, T. and FAINARU, M. (1973). Behçet's disease with decreased fibrinolysis and superior vena caval occlusion. *British Medical Journal*, **1**, 782-783.

CUNLIFFE, W. J. and SUDHAKARAN MENON, I. (1969). Treatment of Behçet's syndrome with phenformin and ethyloestrenol. *Lancet*, **1**, 1239-1240.

DAVIES, J. D. (1973). Behçet's syndrome with haemoptysis and pulmonary lesions. *Journal of Pathology*, **109**, 351-356.

DECROIX, A. G. (1969). Thoracic manifestations of Behçet's syndrome. *Thorax*, **24**, 380.

DUDGEON, J. A. (1961). Virological aspects of Behçet's disease. *Proceedings of the Royal Society of Medicine*, **54**, 104-106.

ENOCH, B. A. (1969). Gangrene in Behçet's syndrome. *British Medical Journal*, **3**, 54.

EVANS, A. D., PALLIS, C. A. and SPILLANE, J. D. (1957). Involvement of the nervous system in Behçet's syndrome: report of three cases and isolation of virus. *Lancet*, **2**, 349-352.

FEIGENBAUM, A. (1956). Description of Behçet's syndrome in the Hippocratic third book of endemic diseases. *British Journal of Ophthalmology*, **40**, 355-357.

FOWLER, T. J., HUMPSTON, D. J., NUSSEY, A. M. and SMALL, M. (1968). Behçet's syndrome with neurological manifestations in two sisters. *British Medical Journal*, **2**, 473-474.

HILLS, E. A. (1967). Behçet's syndrome with aortic aneurysms. *British Medical Journal*, **4**, 152-154.

LEHNER, T. (1967). Behçet's syndrome and autoimmunity. *British Medical Journal*, **1**, 465-467.

MORGENSTERN, N. L. and SHEARN, M. A. (1973). Thymic hyperplasia in Behçet's syndrome. *Lancet*, **1**, 482.

MOWAT, A. and HOTHERSALL, T. E. (1969). Gangrene in Behçet's syndrome. *British Medical Journal*, **2**, 636.

NESTOR, G., BERONIADE, V., CĂRNARU, S. and BADEA, I. (1970). Behçet's disease with renal involvement. *Romanian Medical Review*, **14**, 27-32.

OSHIMA, Y., SHIMIZU, T., YOKOHARI, R., MATSUMOTO, T., KANO, K., KAGAMI, T. and NAGAYA, H. (1963). Clinical studies on Behçet's syndrome. *Annals of the Rheumatic Diseases*, **22**, 36-45.

SEZER, N. (1956). Further investigations on the virus of Behçet's disease. *American Journal of Ophthalmology*, **41**, 41-55.

TURNER, M. E. (1972). Anaesthetic difficulties associated with Behçet's syndrome. *British Journal of Anaesthesia*, **44**, 100-102.

The Author

G. F. Carswell, FRCSE, Senior Urological Registrar.

British Journal of Urology (1976), **48**, 203-206 ©

Preliminary Communication

Cryosurgery for Prostatic Obstruction using Liquid Nitrous Oxide

B. M. WRIGHT
Clinical Research Centre, Northwick Park Hospital, Watford Road, Harrow

Cryosurgery for prostatic obstruction, using liquid nitrogen, was first introduced in 1966 by Soanes and Gonder. Although the procedure has since had considerable vogue in the USA its use in this country, after an initial period of enthusiasm (Marshall, 1968; Gill *et al.*, 1970; Green, 1970) has been almost abandoned. A leading article in the *British Medical Journal* (1971), although it admitted that cryosurgery had some advantages, such as not requiring general anaesthesia, causing no haemorrhage and allowing early ambulation, concluded that the reported success rate of 60% to 80% was not enough to compensate for frequent complications such as slough retention and injury to surrounding tissues.

The use of liquid N_2O instead of nitrogen was introduced in Italy by Sesia, Ferrando and Riggi (1968) who pointed out its many practical advantages over N_2, such as its easy availability, simplicity of use and much greater safety.

A cryosurgical probe for prostatic obstruction using liquid N_2O was first constructed by the author in 1968 before the publication of Sesia's work in English. Owing to the unfavourable climate of opinion it was difficult to persuade surgeons to try the method, so that initial progress was very slow but the probe is now in use in a number of centres in this country and abroad for elderly and infirm patients with prostatic obstruction. Although the results so far are not quite as good as those claimed by Sesia the instrument and operating technique are a good deal simpler.

Construction and Mode of Action of Cryoprobe

The construction of the probe is shown in the Figure.

The probe is fed with liquid N_2O from an inverted cylinder held in a special stand. The gas-feed tube (8) is inserted and the tapers (6) and (16) engaged. The cylinder valve is opened and the flow regulated with the valve (9). Liquid N_2O emerges from the end of the feed tube and evaporates and cools the tip of the probe. The gas returns along the gap between the feed tube (8) and the inner tube (3) and emerges through the side arm (7). Initially the flow can be very high but as the tissues freeze and insulate the tip liquid N_2O begins to appear at the side arm and N_2O snow is formed. The flow is regulated so that a small amount of liquid and snow are always appearing; if no liquid at all appears, freezing may be inadequate, while excessive flow produces submaximal freezing. The frozen zone grows very rapidly at first but growth gradually slows down until, after about 10 min, the zone gets no larger however long freezing is continued. At the end of the freezing period the gas is turned off and the feed tube withdrawn. The probe can then be freed by instilling 20 to 40 ml of hot water with a syringe through the long needle (17).

Operative Procedure

Patients are prepared as for cystoscopy and the operation can be performed under local anaesthesia with sedation. If the patient already has a catheter it should be retained; if not, one should be inserted and the bladder distended with 200 to 300 ml of warm sterile water to prevent damage to its walls. It is not necessary to use air, as recommended by Sesia and others, since very little ice is formed in water at 37°C because of the powerful convection currents that are generated.

The position of the freezing zone is determined per rectum by palpating the button (4) which should be just below the apex of the prostate. The probe may be inserted further without harm but if it is too far out the membranous urethra may be damaged. As soon as freezing starts the probe becomes fixed and it is no longer

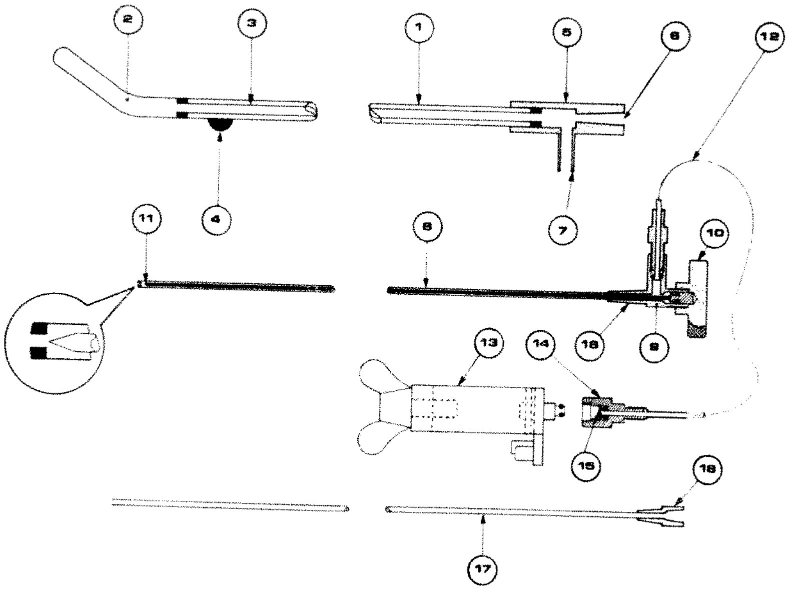


Figure. The probe is a blind ended steel tube (1) 6 mm in diameter, similar in shape to a Liston sound. The terminal 5 cm (2) are thin walled while the stem has an inner concentric tube (3) forming an air filled cavity wall. A button (4) is attached to the probe about 1 cm from the thin-walled portion and projecting about 3 mm from it. A plastic T-piece (5) on the butt end has a female Luer taper (6) to accept the gas feed unit and a side arm (7) for the escaping gas. The liquid is fed in through a stainless tube (8) which is a free fit in the inner tube (3) and reaches into the end cavity (2) of the probe. It carries a flow control valve (9) with an adjusting knob (10) which operates on a long needle (11) extending to the tip of the feed tube. The unit is connected by a length of flexible nylon tubing (12) to a pin-indexed N_2O cylinder fitting (13). The cylinder end of the tubing is secured with a knurled nut (14) containing a gauze filter (15). The valve (9) carries a male Luer taper (16) which fits into the female taper (6) in the butt of the probe. A long steel hollow needle (17) with a male-female Luer fitting (18) is also supplied.

necessary to hold it or to keep a finger in the rectum. Although the frozen zone in the prostate can readily be felt the rectal wall is never perceptibly cool. At the end of the freezing period the gas feed unit is removed and the probe thawed out as described and it can then be easily withdrawn and replaced by a self-retaining catheter. The prostate itself does not thaw completely for about 10 min. The catheter should not be removed for 10 days and it may be necessary to return it for up to 3 weeks before flow is restored. If the operation is not successful a second operation can be performed and is sometimes successful. The patient can be ambulant almost immediately and can return home with an indwelling catheter if conditions are suitable.

Results

The first 3 operations were performed at Hammersmith Hospital in 1971.

The first patient was aged 78 and had been catheterised for 2 months following acute retention because he was considered by reason of his age and a long history of cardiac ischaemia to be unfit for surgery. Postoperatively he had some pain and developed a urinary infection but was discharged after 15 days passing water freely. When last heard of 9 months later he was still able to pass water.

The second patient, aged 73, also had a long history of cardiac ischaemia and had been catheterised for 2 years. He suffered no postoperative pain but also developed a urinary infection. When last heard of 2 years later he was still passing water freely, though very senile.

The third patient was 74 and had had a recent coronary thrombosis. He had a large prostate and there was some doubt whether the probe then in use was long enough to pass right through it. In the event, the operation was unsuccessful. Some weeks later he was fit enough for trans-urethral resection (T.U.R.) which was performed without difficulty.

Since then work has been carried out at Northwick Park Hospital (Elton and Wright, 1974), at the Onze Lieve Vrouwe Hospital, Amsterdam, at the National University Medical College, Busan, Korea, at Chase Farm Hospital, Enfield and at the Royal Naval Hospital, Haslar. All these centres have obtained encouraging results which they will be reporting in due course. Out of a total of 82 patients, 54 % or 66 % were relieved of obstruction and there have been no relapses so far or any complications of the kind that often follow T.U.R. or prostatectomy, or cryosurgery using liquid N_2.

All the patients were old, the oldest, in whom the operation was successful, being 102. There were 6 deaths from intercurrent diseases associated with old age within 10 days of operation. Most of the remaining patients were treated successfully by open operation or T.U.R. unless they were so unsuitable for operation that they had to return to a catheter life. Successful results were obtained in some cases of prostatic carcinoma but the operation was, of course, only palliative treatment.

Discussion

These results together with those of Sesia *et al.* (1968, 1970) suggest that prostatic cryosurgery with liquid N_2O is an effective and exceptionally safe procedure. The complications that have caused cryosurgery with liquid N_2 to fall into disrepute are not seen because of the limited freezing power of the probe. The operation may be likened to a limited T.U.R. but it does not require such a skilled and experienced operator.

The inherent safety of the procedure results from the higher boiling point of N_2O, $-89°C$ compared with $-196°$ for N_2, which means that an equilibrium situation is reached where no further extension of freezing will occur however long cooling is continued. In addition, increasing the rate of flow of N_2O above the optimum decreases the freezing power of the probe because no more liquid can be evaporated and the increased flow of warm liquid brings more heat into the probe. A similar effect was noted with an N_2O cooled neuroprobe (Wright, 1971).

The present shape of the probe has been found to be the easiest to insert but it is possible that a straighter probe would be more effective in some cases where there is a large middle lobe. Work on the best shape of probe and the reasons for failures is still required. The locating button is an important feature and it is essential that it should be prominent or it may not be palpable PR in an obese subject. Provided the probe is well lubricated and inserted with care the button causes no harm.

Sesia *et al.* (1970) have reported on the results of 142 operations on adenomas and carcinomas of the prostate together with 5 cases of sclerosis of the bladder neck. They have claimed "excellent" results in 74 % and "good" in 16 % with a follow-up of 3 to 13 months, giving a complete failure rate of only 10 %. These results are at least as good as those obtained with liquid N_2 and there were virtually no postoperative complications.

The main difference between Sesia's technique and ours is that he uses gaseous N_2O and liquefies it by refrigeration. This substantial added complication is apparently needed because of contaminants in the N_2O he uses which are not met with in the UK.

Sesia also normally freezes for 2 periods of 15 to 20 min, with an interval of 6 min. He has no method of thawing the probe so his operation must take 40 to 45 min, instead of 10 to 15. He also retains the catheter "for an average of 4 weeks" instead of 8 to 10 days. Some workers are now trying out this technique but it is too early yet to say whether there is any improvement in the results.

Up till now cryosurgery has generally been reserved for those who are unfit for either an open operation or a transurethral resection of the prostate. In view of the simplicity and safety of this procedure, however, when liquid N_2O is used, it would now seem justifiable to reconsider cryosurgery not only for the unfit but also as an alternative for patients who are fit for normal surgery.

Further experience, assessing both the clinical effectiveness and the impact of such a simple technique on hospital waiting lists is now awaited.

Summary

The history of the use of liquid N_2O for prostatic cryosurgery is briefly reviewed and an account given of a new simple instrument.

Details are given of the first 3 operations and of the results of another 82 performed at a number of different centres.

Relief of acute or chronic obstruction was obtained in about two-thirds of the patients, all of whom were elderly and unfit for conventional operations.

There were no serious complications attributable to the operation and it was suggested that it would now be justifiable to offer it, as an alternative, to patients who are fit for conventional surgery.

I am indebted to Professor Ralph Shackman, FRCS, for carrying out the first 3 operations and to Mr A. Elton, FRCS, Dr G. Bosman, Professor H. J. Moon, Mr Max Pemberton, FRCS and Surgeon Captain N. J. Blacklock, RN, FRCS for their willingness to try the procedure. I am grateful to Mr J. Larsen and the Department of Medical Illustration for the Figure.

The probes used at Northwick Park Hospital and Amsterdam were made by the author at the National Institute of Medical Research and in the Bioengineering Division of the Clinical Research Centre. The other centres used a commercial version made by Messrs Spembly Ltd., Industrial Estate, Newbury Road, Andover, Hants, SP10 4DR.

References

British Medical Journal. (1971). Freezing the prostate, **2**, 5-6.

Elton, A. and Wright, B. M. (1974). Price of prostatectomy. *British Medical Journal*, **3**, 808.

Gill, W., Fraser, J., Long, W. and Lee, P. (1970). An experience with cryoprostatectomy. *Surgery, Gynecology and Obstetrics*, **131**, 877-884.

Green, N. A. (1970). Cryosurgery of the prostate gland in the unfit subject. *British Journal of Urology*, **42**, 10-20.

Marshall, A. (1968). Cryogenic surgery of the prostate. *Proceedings of the Royal Society of Medicine*, **61**, 1139-1142.

Sesia, G., Ferrando, U. and Riggi, G. (1968). A new apparatus for use in the cryotherapy of prostate obstruction. *International Surgery*, **49**, 330-338.

Sesia, G., Ferrando, U. and Laudi, M. (1970). The use of nitrous oxide as a freezing agent in cryosurgery of the prostate. *Internationsl Surgery*, **53**, 82-90.

Soanes, W. A., Gonder, M. J. and Shulman, S. (1966). Apparatus and technique for cryosurgery of the prostate. *Journal of Urology*, **96**, 508-511.

Wright, B. M. (1971). Nitrous-oxide-cooled neurosurgical cryoprobe. *Lancet*, **1**, 951-952.

The Author

B. M. Wright, MA, MB, Member of Scientific Staff, MRC.

British Journal of Urology (1976), **48**, 207-209 ©

Latent Carcinoma of the Prostate: the Probability of Identifying Small Lesions in Routine Histology

G. S. DELIDES, G. BALTOPOULOS and N. X. PAPAHARALAMPOUS
Department of Pathology, University of Athens

The frequency of clinically unsuspected "latent" or "occult" carcinoma of the prostate is estimated to be approximately 10% (Miller and Seljelid, 1971). Apart from frankly carcinomatous lesions, areas of marked or slight atypia have been described as representing an *in situ* phase of prostatic carcinoma. The differences in the reported frequencies of such lesions depend on whether these areas of atypia are classified as carcinoma or not (Miller and Seljelid, 1971). The lesion may occupy a large part of the surgical specimen but is usually so small as to escape notice on gross examination, being identified only microscopically. The majority of both carcinomatous and *in situ* lesions are located in the periphery of the prostate and their demonstration in routine histological sections is unlikely in view of their small size, unless an impracticable number of blocks are taken for examination.

This study reports the frequency of "occult" carcinoma in the surgical material of the University of Athens and suggests a method of taking blocks from prostatectomy specimens in order to increase the probability of demonstrating these lesions histologically.

Materials and Methods

In the 25-year period 1949-73, material from 3,072 cases of open prostatectomy with a clinical diagnosis of benign prostatic hyperplasia was examined by routine histology in the Department of Pathology in the University of Athens. The tissue was fixed in 4% formaldehyde and processed to wax. Sections were cut at 5 μ thickness and stained with haematoxylin and eosin.

Results

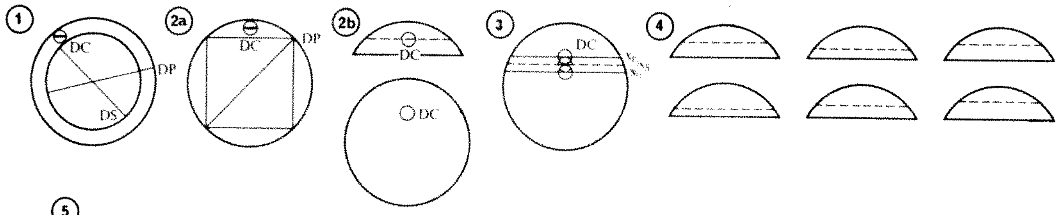
Of the 3,072 cases examined 117 (4%) revealed frank carcinoma of the prostate. The tumour was large and identifiable on gross examination. In 74 cases a small focus of abnormality was originally reported being classified as a small focus of carcinoma (15 cases), carcinoma-*in situ* (23 cases) or areas of atypia (36 cases).

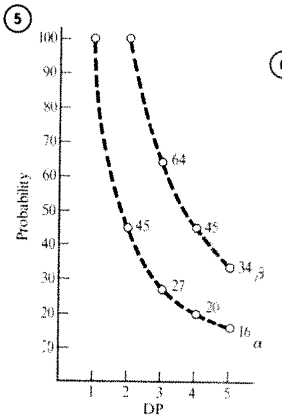
These 74 cases were re-classified to consist of 27 cases of occult carcinoma (0·88%) and 47 cases of marked or slight atypia. Of these 74 cases the lesions in 71 (96%) were situated in the periphery of the excised nodules. The mean diameter of the lesions ranged from 2·7 mm to 0·275 mm (mean 1·072 mm ± 0·2 mm).

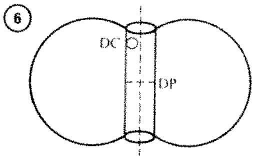
Discussion

While the characterisation of a "small lesion" as carcinomatous or "precancerous" depends sometimes on the examining pathologist, the identification of such a lesion with a diameter of 1 mm within a hyperplastic nodule is a matter of chance, if the lesion is not obvious by gross examination.

The probability of identifying the lesion depends on the surface area of tissue included in the histological section.







Equation 1. $Px = 1{\cdot}5\frac{(x_1 - x_0)}{DP} - 2\frac{(x_1^3 - x_0^3)}{DP^3}$

Equation 2. $Px = \frac{1}{DP^3}\left(DP^3(x_1 - x_0) - 2(x_1^3 - x_0^3)\frac{\alpha}{100}\right) + $

$+ \frac{1}{DP^3}\left(0{\cdot}5DP^2(x_i - x_0)(100 - \frac{\alpha}{100})\right)$

Equation 3. $Px = \frac{1}{6}\left[\frac{1}{(3-\sqrt{2})(2-\sqrt{2})}\left(24\frac{(x_1 - x_0)}{DP} - 32\frac{(x_1^3 - x_0^3)}{DP^3}\right)\right]$

Under the condition $\frac{DP}{2\sqrt{2}} \leqslant x_0 < x_i \leqslant \frac{DP}{2}$

Equation 4. $Px = \frac{DC}{DP - DC}$

Figs. 1-6.

If a representative prostatic nodule is considered spherical in shape with diameter DP (Fig. 1) then a randomly taken histological section gives a surface for microscopy included within a circle.

Knowing that the majority of latent carcinomata are located in the periphery of the nodules, we can consider the carcinomatous lesion of diameter DC (Fig. 1) to be also spherical and located outside a sphere of diameter DS homocentric to sphere DP (DS = DP − DC). Thus the diagnostically valuable area of a single section is limited to that included between 2 homocentric circles (Fig. 1).

Practically it is almost impossible to cut out from a prostatic nodule a central sphere. It appears easier to cut 6 segments of the sphere so that the central part remains as a cube inscripted to the sphere, the diagonal of the cube and the diameter of the sphere being identical (DP) (Fig. 2a). A section taken through each segment, parallel to its base, gives a diagnostically useful surface included within a circle (Fig. 2b). Since this has a greater diagnostically useful area than the randomly taken section through the sphere DS (Fig. 1) the chances of exposing the lesion are greater. While a section through the centre of a nodule of 5 cm diameter gives a diagnostically useful surface equal to 701·1 mm², a section through the segment by the side of the cube gives a surface of 987·5 mm².

If the carcinomatous lesion DC is located somewhere within the nodule it can be identified if a slice from the nodule that includes the lesion and has a thickness equal to DC is bisected by the histological section (Fig. 3). The lesion DC can be located in either side of the section. The effective slice thickness DC can be defined by $X_1 - X0$. X1 and X0 are distances from the centre of the sphere (nodule). Xs is the distance from the centre of the sphere at which the section is taken.

$X1 = Xs + \frac{DC}{2}$, $X0 = Xs - \frac{DC}{2}$ (Wilkinson and Hause, 1974).

The conditional probability of identifying such a lesion randomly located within the sphere, can be calculated by equation 1 (Wilkinson and Hause).

If we accept that the lesion is located in the periphery of the nodule then equation 1 must be corrected as equation 2 where *a* is the frequency of the location of the lesion in the periphery. (In our material the frequency is 96% so $\frac{a}{100} = 0{\cdot}96$ and $100-\frac{a}{100} = 0{\cdot}04$.)

If the slice is taken parallel to the base of the spherical segment (to the side of the inscripted cube) then the conditional probability of identifying the lesion can be calculated by equation 3 and it is greater than that of equation 2.

If sections are taken through the 6 segments of the sphere then the probability is multiplied by 6 and is greater than that of 6 randomly taken sections. So the recommended way of taking the sections is demonstrated in Figure 4.

Even by taking the sections with the recommended way the probability is still very small.

For a nodule 5 cm in diameter, in the periphery of which there is a lesion 1 mm in diameter the probability of identifying the lesion in 6 parallel randomly taken sections is 4·98%, whereas in 6 sections taken in the way here recommended it is 16%.

In Figure 5 is demonstrated the percentage probability of identifying lesions 1 and 2 mm in diameter in relation to the dimensions of the nodule.

Sometimes the surgical specimen has a shape which can be considered as two spheres joined by a cylinder (Fig. 6). Then the probability of identifying it can be calculated by equation 4 (Wilkinson and Hause, 1974) where DP is the size of the cylinder along a line perpendicular to the surface of a section taken along the longitudinal axis.

This probability must be added to those calculated from the joined spheres.

Summary

In 3,072 open prostatectomy specimens covering a 25-year period 117 (4%) showed frank carcinoma.

A further 74 cases showed areas of occult carcinoma or atypical hyperplasia. These focal lesions had an average diameter of 1 mm and 96% were situated in the peripheral regions of the specimen. In view of the situation of these lesions and their small size, an improved method of taking blocks for histological sections from prostatectomy specimens is proposed, resulting in an increased probability of demonstrating the areas of occult malignancy.

We should like to thank Dr C. Charalambidis, Department of Statistics, Faculty of Science, for his assistance in the preparation of this paper.

References

MILLER, A. and SELJELID, R. (1971). Cellular atypia in the prostate. *Scandinavian Journal of Urology and Nephrology*, **5**, 17-21.

WILKINSON, E. J. and HAUSE, L. (1974). Probability in lymph node sectioning. *Cancer*, **33**, 1269-1274.

The Authors

TY COLLEGE OF MEDICINE LIBRARY

G. S. Delides, MD, Senior Lecturer in Pathology.
G. Baltopoulos, MB, ChB, Research Assistant.
N. X. Papaharalampous, MD, Professor of Pathology.

British Journal of Urology (1976), **48**, 210 ©

Short Case Report

Malignant Testicular Lymphoma in Brothers

Malignant testicular lymphoma is reported in siblings. In one case bilateral tumours occurred non-simultaneously: the patient survived 66 months, with 57 months between the onset of disease on either side.

Case 1

E. D. (26.6.1900).
7 months painless swelling left testis.
Left orchiectomy.
Irradiation of regional lymph nodes.
Histology: malignant round cells of lymphoblastic type (Fig. 1).
5 years later, swelling right testis.
Right orchiectomy and irradiation.
Pathological fracture neck of femur.
Patient died.
Histology: identical.
Autopsy revealed a solitary femoral metastasis.

Case 2

F. D. (26.6.1897).
3 months testicular swelling and right-sided abdominal mass.
I.V.P., non-functioning right kidney.
Right orchiectomy.
Histology: pleomorphic lymphoblastic cell type (Fig. 2).
Patient died soon after operation.

Comment

Collins and Pugh (1964) noted a 0·5% familial incidence in teratoma and seminoma. Echert and Smith (1963) stated testicular lymphoma is a primary lesion; Abell and Holtz (1968) stress it is a part of generalised manifestation.

The interesting feature in our case is the familial aspect and the long interval before tumour appeared in the remaining testis in Case 1.

B. L. S. GALLAGHER and A. I. HASHMAT
Royal Infirmary, Bradford, Yorks

References

ABELL, M. R. and HOLTZ, F. (1968). Testicular and paratesticular neoplasms in patients 60 years of age and older. *Cancer*, **21**, 852-870.

COLLINS, D. H. and PUGH, R. C. B. (1964). Classification and frequency of testicular tumours. *British Journal of Urology*, **36**, Supplement 1-11.

ECKERT, H. and SMITH, J. P. (1963). Malignant lymphoma of the testis. *British Medical Journal*, **2**, 891-894.

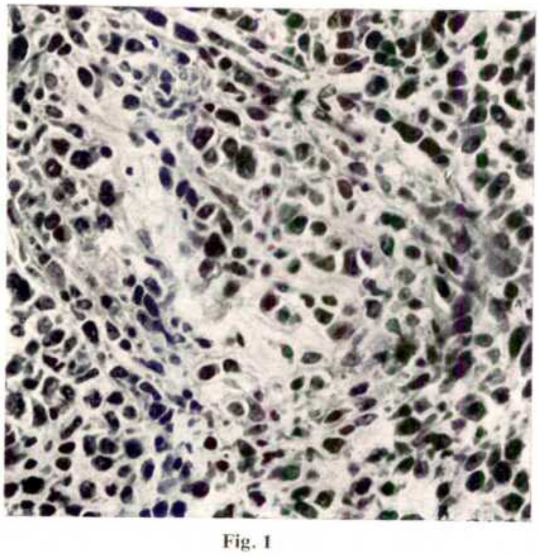


Fig. 1

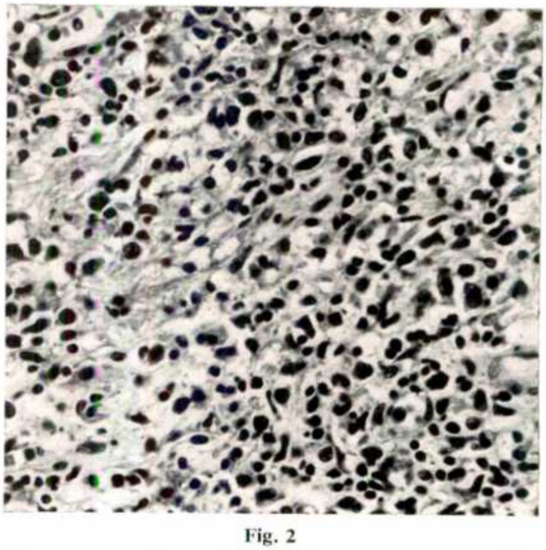


Fig. 2

British Journal of Urology (1976) **48**, 211-218 ©

Introital Bacterial Flora—Effect of Increased Frequency of Micturition

JOHN M. SEDDON, ANDREW W. BRUCE, PAUL CHADWICK and DONNA CARTER
Departments of Urology and Bacteriology, Queen's University, Kingston, Ontario, Canada

Recent urological literature contains many publications on the subject of recurrent lower urinary tract infection in the female. It is generally accepted that invasion of the lower urinary tract with pathogens occurs via the urethra (Stamey, 1973). The nature of the bacterial flora of the urethra will therefore have some bearing on an individual's susceptibility to urinary infection. The bacterial flora of the urethra has been shown to be reflected by the flora of the introitus (Bruce *et al.*, 1973). It follows that introital organisms may be of significance in the pathogenesis of urinary tract infection. This assumption is complicated by the occurrence of introital pathogens in normal subjects (O'Grady *et al.*, 1970), although a higher incidence of pathogen isolation has been encountered in the patient group (Marsh, Murray and Panchamia, 1972; Bailey *et al.*, 1973).

By the term potential urinary pathogens, most workers are referring to enterobacteria only. Bruce *et al.* have pointed out that *Streptococcus faecalis* is commonly isolated from the introitus and should also be considered a potential urinary pathogen (Bruce *et al.*, 1973).

The isolation of pathogens from the introitus is considered to be significant only when such isolation reflects introital colonisation rather than contamination (Stamey, 1973). Initially attempts to differentiate colonisation from contamination involved repetitive qualitative culturing of the introitus (Stamey, 1973); the impractibility of this approach led other workers to explore the value of quantitative culture methods applied to one or a few samples (Marsh *et al.*, 1972; Motzkin, 1972; Bailey *et al.*, 1973; Elkins and Cox, 1974).

The quantitative techniques have involved the use of a cotton swab, the organisms being transferred to a fluid medium such as saline or nutrient broth, by agitation of the swab in the medium. The medium is then treated in the same way as a urine sample, so that an organism count in numbers per ml is obtained. Colonisation is suggested by counts exceeding 1,000 or 2,000 organisms per ml depending on the technique used. How the criteria of significance became attached to these figures is not explained in the literature!

Over the past 2 years we have used a calcium alginate swab which dissolves completely in 2 ml of 1% sodium hexametaphosphate solution (Colab Laboratories, Chicago). We felt that by using this type of swab, the transfer of organisms from the swab to the fluid medium would be complete and its use would eliminate part of the sampling error of other methodologies.

Using this technique a study was designed to evaluate:

1. Comparison of the single qualitative and quantitative swabs and repetitive qualitative and quantitative culturing in determining colonisation.
2. The effect of frequency of micturition on the nature of the introital organisms cultured.
3. The effect of sampling time, in relation to last voiding, on the number of organisms retrieved.

Methods and Materials

20 single female volunteers, all nursing personnel, ages ranging from 19 to 26 years of age, underwent the study. Each subject completed a preliminary questionnaire which dealt with past urological and gynaecological history, present urological and gynaecological symptomatology and

Table I

Illustration of Data collected on each Subject

Control Period (normal voiding)		
Day 1	MSSU	
	Introital swab	1—1 hour post-voiding 1—4 hours post-voiding
Day 2	Introital swab	1—1 hour post-voiding 1—4 hours post-voiding
Study Period (voiding every 2 hours)		
Day 3	Introital swab	1—1 hour post-voiding 1—2 hours post-voiding
Day 4	Introital swab	1—1 hour post-voiding 1—2 hours post-voiding
Day 5	Introital swab	1—1 hour post-voiding 1—2 hours post-voiding
MSSU		

The 5 days to run consecutively.
Urine to be collected without preparation.
No menstruation during the 5 days.

Table II

Percentage Incidence of various Organisms in 200 Introital Cultures

Organism	%
Coagulase negative staphylococcus	25
Lactobacillus	20
Non-haemolytic streptococcus	12·5
Enterobacteria	15
Streptococcus faecalis	10
Other	17·5

information regarding relevant medications. Volunteers with known urological abnormalities and/or a history of urinary tract infection within 6 months of the study period were excluded.

For each subject the experimental period extended over 5 consecutive days (Table I). They were asked to avoid intercourse, the use of local creams and sprays. etc., during the 5 days and the period was timed so as not to coincide with menstruation. To study the effect of frequency of micturition on the introital flora retrieved, each subject acted as her own control, thus minimising other variables. During the first 2 days (control period), the subjects were requested to void normally and to note their voiding times. During the last 3 days (study period), they were requested to void every 2 hours and at least once during the night. A record of voiding times was kept during this period.

Introital Cultures

2 introital cultures were collected each day. During the control period one was obtained 1 hour after voiding and one 4 hours after voiding, each in relation to separate acts of micturition. During the study period cultures were taken 1 hour and 2 hours after separate acts of micturition. 10 introital cultures were thus obtained on each subject. All swabbing procedures were performed by a trained urological nurse using a standard technique (Bruce *et al.*, 1973).

Mid-stream Urine Cultures

Each volunteer was allowed to collect her own mid-stream urine samples, preliminary washing of the genital area with antiseptic being omitted. 2 specimens were obtained from each subject, one at the beginning of the experiment and one at the end. No volunteer showed 10,000 or more organisms per ml in either mid-stream specimen.

Bacteriological Methods

All specimens were sent immediately to the Microbiology Laboratory. All organisms growing from these specimens were recorded. Enterobacteria and enterococci were identified to species level; staphylococci were characterised by their coagulase reaction; corynebacteria and lactobacilli were identified to generic level only.

Results

Bacteriological Data

10 introital swabs were collected from each volunteer representing a total of 200 introital cultures.

Table III

Illustration of Data retrieved on 1 Subject (C11)

Control Period (introital cultures)

	1 hour	4 hours
Day 1	7,500 *E. coli* 6,000 klebsiella	500 *E. coli* 2,000 klebsiella 5,000 lactobacilli
Day 2	8,500 *E. coli*	3,900 *E. coli* 40 klebsiella

Study Period (introital cultures)

	1 hour	2 hours
Day 3	2,700 *E. coli* 1,200 enterobacteria 1,800 staphyloccoci 2,600 streptococci 100,000 lactobacilli	1,500 *E. coli* 1,400 staphyloccoci 2,000 streptococci 100,000 lactobacilli
Day 4	1,500 *E. coli* 200 klebsiella 100,000 lactobacilli	3,600 *E. coli* 100 klebsiella 6,500 streptococci 6,500 staphylococci 100,000 lactobacilli
Day 5	200 *E. coli* 500 streptococci	200 *E. coli* 400 klebsiella

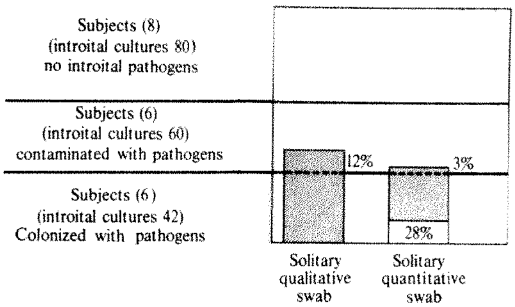
Table II shows the frequency of isolation of various types of organisms and the results are in agreement with previous observations (Bruce *et al.*, 1973). The organisms most frequently isolated were coagulase negative staphylococci and lactobacilli. Potential urinary pathogens were isolated in 25% of the 200 introital cultures. We have considered *Streptococcus faecalis* as a potential urinary pathogen.

With regard to the quantitative aspect of the culture, a significant count of any pathogen was taken to be 1,000 or more organisms/ml. Table III illustrates a representative set of culture results obtained from 1 subject over the 5-day period.

We noted that the bacteria isolated on any one day, in any one subject, could vary in nature and number. Frequently pathogens were isolated in "significant" counts, only to be absent in the flora sampled some hours later. This table also illustrates that the time of sampling in relation to last voiding does not appear to produce a constant effect on the number of organisms retrieved.

Quantitative Swab Evaluation

Analysis of our data showed that if a pathogenic organism was isolated from all 4 swabs taken during the initial 2 day control period, then all subsequent swabs also yielded the pathogen. When a pathogen was isolated from only 1, 2 or 3 of the initial 4 swabs it could not be recovered constantly from later swabs. Isolation of a pathogen from all 4 swabs over a 48-hour period was therefore taken to indicate colonisation. Obviously greater diagnostic accuracy would be achieved by increasing the number of swabs collected during the 48-hour period. From our data however, we felt that 4 cultures evenly spaced in time, formed an adequate minimal number. The number of organisms recovered was not relevant to this definition. Table IV illustrates a typical example of colonisation with *Escherichia coli*.



Solitary qualitative swab – false + ve rate 12%
false – ve
Solitary quantitative swab – false + ve 3%
false – ve 28%

Fig. 1. Accuracy of the solitary qualitative and solitary quantitative swab in identifying the colonised state. The shaded areas represent colonisation as identified by either swabbing techniques.

Unfortunately the above accurate diagnostic methodology is impractical in the clinical situation. The value of the solitary swab, cultured either qualitatively or quantitatively must therefore be assessed. Analysis of the data with regard to the ability of a single quantitative swab to identify colonisation is illustrated in Figure 1. In 8 subjects representing 80 cultures, no pathogens were isolated during the 5-day period. 6 subjects representing 60 introital cultures showed intermittent pathogen isolation which we regarded as contamination. The final 6 individuals showed colonisation as defined by our criterion. Of 42 introital cultures obtained from these 6 subjects while they were colonised, 12 (28%) yielded less than 1,000 organisms per ml (false negatives). This gives a 95% confidence limit of 15% to 43%. 5 of the 140 cultures (3%) from non-colonised individuals grew 1,000 or more organisms per ml (false positives). A 95% confidence limit on this rate would have an upper limit of 7%. It should be noted that the false positive rate with a solitary qualitative swab in this study was 12% with a 95% confidence limit of 7·2% to 18·6%.

Frequency of Micturition

All subjects maintained a 2-hourly voiding pattern during the last 3 days of the study.

3 of the 20 volunteers were found to be colonised with pathogens during the control period. No reduction in count numbers, or disappearance of the pathogen was noted in these 3 subjects during the period of 2-hourly micturition (Table IV).

Of the 17 subjects free of pathogen colonisation during the control period, 3 became colonised with pathogens during the study period. An example is given in Table V. This is a highly significant result. Calculations, based on the bacteriological data retrieved from the 17 subjects, reveal that the probability of 4 consecutive swabs isolating a pathogen by chance alone, would be less than 0·0001. (Binomial test, Poisson test.)

Questionnaire Data

Comparison of the information obtained from the questionnaire with the bacteriological data revealed little of significance.

As shown in Table VI, 5 of the subjects had a past history of urinary tract infection, 2 having had such an episode within a year of the study. Using the criterion of colonisation previously described, 3 of these 5 girls (C11, C14, C23), were colonised with pathogens. As can be seen in Table VI these were not the ones with the recent history of infection.

The questionnaire data also revealed 8 girls were on contraceptive medication and 7 engaged in regular coitus. 2 subjects had a past history of enuresis. No significant correlations were noted between the bacteriological data and coitus, contraceptive medication or a past history of enuresis.

Discussion

Elkins and Cox (1974) have noted variation in introital flora when subjects were followed over a period of months. In previous reports culturing has been performed at weekly intervals (Stamey,

Table IV

Example of a Subject colonised with *Escherichia coli*

Control Period (introital cultures)

	1 hour	4 hours
Day 1	1,300 *E. coli*	14,000 *E. coli*
Day 2	160 *E. coli*	12,000 *E. coli*

Study Period (introital cultures)

	1 hour	2 hours
Day 3	27,000 *E coli*	1,400 *E. coli*
Day 4	100,000 *E. coli*	100,000 *E. coli*
Day 5	1,200 *E. coli*	2,000 *E. coli*

Table V

Example of a Subject who became Colonised with a Pathogen during the Period of Frequent Voiding

Control Period (introital cultures)

	1 hour	4 hours
Day 1	...	...
Day 2	...	...

Study Period (introital cultures)

	1 hour	2 hours
Day 3	...	...
Day 4	4,000 *E. coli*	20 *E. coli*
Day 5	2,500 *E. coli*	2,000 *E. coli*

1973; Bruce *et al.*, 1973). To our knowledge, this is the first time that such introital culturing has been performed intensively over a period of days. We were surprised to note the tremendous variation in the number and type of organisms. It is not surprising therefore, that variability should be noted over weeks and months. With such daily variation, the accuracy of diagnosis of colonisation in previous reports (Stamey, 1973) based on weekly or monthly sampling, is clearly questionable. Serological typing of organisms does not increase the accuracy since the pathogens whether responsible for introital contamination, colonisation or urinary tract infection are all derived from the same source, the large bowel. Serological typing merely confirms this fact. It contributes no information as to the nature of the flora on the introitus during the long intervals between cultures.

When we began to analyse the data from the volunteers it became obvious that a clear definition of what we meant by colonisation was necessary. Previous investigators have referred to colonisation versus short-term contamination of the introitus (Stamey, 1973). The use of the term colonisation implies growth of organisms whereas contamination implies a continuing reduction in number from the time of contamination to complete disappearance. We feel this interpretation is too simple. To our mind the continued presence of pathogens on the introitus probably depends on a number of factors.

1. increase in frequency and degree of contamination,
2. growth of pathogens on the introitus,
3. decreased efficiency of introital bacterial clearing mechanisms,
4. unknown factors.

Persistence of pathogens may result from 1 or more of these factors being operative. Clearly one could have continued presence of pathogens without there being actual growth of pathogens on the introitus. Therefore by the term colonisation we mean persistence of pathogens and are not necessarily implying growth. We found that in a given individual, if the pathogens persisted over 48 hours, conditions were suitable for their presence throughout the experiment. As will be discussed later, in some subjects introducing 1 factor in the form of increased frequency led to persistence of pathogens.

How long does "colonisation" have to be present for it to become significant, *i.e.* produce infection. Stamey (1973) has shown that this time period in some subjects may be in the order of

Table VI

Subjects having a Past History of Urinary Infection with Number of Episodes and Dates

Subjects (5)	Number of episodes	Dates
C8	1	Oct. 1973
C9	1	Aug. 1973
C11	2	June 1954 Feb. 1969
C14	1	Sept. 1972
C23	1	Aug. 1960

Table VII

Some of the Factors that have been Implicated in producing Susceptibility to Lower Urinary Tract Infection in the Female

Trauma	Mechanical:	Coitus[12]
		Instrumentation
	Chemical	Bubble bath [13]
		Soap[14]
Inflammatory	Post-menopausal atrophic vaginitis	
	Ammoniacal dermatitis[15]	
	Para-urethral gland infection [16]	
Urodynamic	Meatal stenosis[17]	
	Distal urethral stenosis[18]	
	External sphincter spasm[19]	
	Uninhibited neurogenic bladder[20]	
Allergy[21]		
Psychogenic		

weeks. It is possible that this time period differs from individual to individual and probably depends to some extent on the presence of other factors that have been implicated in the production of infection (Table VII). It is not hard to imagine that in certain circumstances, the presence of pathogens over a period of hours, as in the contaminated state, would be all that is necessary. Logically however, the longer the pathogens are present on the introitus, the greater the likelihood of infection occurring and hence the clinical importance of identifying continued pathogen presence.

Although the solitary quantitative swab as used to determine colonisation, has a slightly lower false positive rate compared with the solitary qualitative swab (3% to 12%). its principal disadvantage is the high false negative rate introduced with its use (28%). As previously described in our study, a significant quantitative swab was one showing a growth of at least 1,000 organisms per ml. It should be noted that this significance criterion is much lower than that recommended by Elkins and Cox (1974) or Motzkin (1972). The methodology used by Cox involved the use of a fluid medium volume of 5 ml in the transference of organisms from the swab to the fluid phase. In our study the volume used was 2 ml. This dilution difference means that Cox's significance criterion of 1,000 organisms/ml represents a 2·5 × increase over the one used in this study. Motzkin (1972) used a volume of 2 ml in the transference of organisms from the swab to the fluid phase. However his significant cultures were taken to be those showing a growth of 2,000 organisms/ml. It follows therefore, that using their methodology, a much higher incidence of false negatives is to be expected with the use of a solitary quantitative swab. Our results suggest that the solitary quantitative swab is of little use in identifying the colonised state regardless of the methodology used.

The solitary qualitative swab is a practical method of identifying all colonised individuals. However, it should be recognised that a certain number (12% in this study) of contaminated individuals will also show apparent colonisation (Fig. 1).

Frequency of micturition appears to be the only variable introduced during the study period We have excluded other variables by the design of the experiment and close questioning of the volunteers following its completion. We believe that the increased frequency of micturition is responsible for the change in introital flora noted. After reviewing Dr Gleason's film, it is not

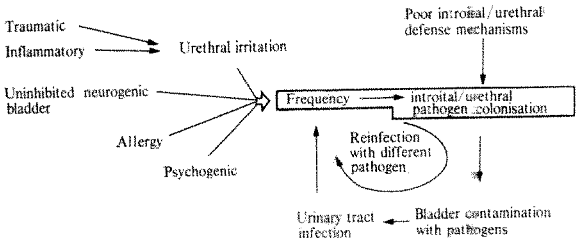

Traumatic
Inflammatory
Urethral irritation
Poor introital/urethral defense mechanisms
Uninhibited neurogenic bladder
Frequency
introital/urethral pathogen colonisation
Allergy
Psychogenic
Reinfection with different pathogen
Urinary tract infection
Bladder contamination with pathogens

Fig. 2. Possible interrelationship of various factors responsible for lower urinary tract infection in the female and the recurrence of infection after treatment

hard to imagine how contamination of the introitus with large bowel flora occurs during voiding. It is suggested that frequency of micturition would increase the rate of contamination and produce colonisation. Because of the strict criteria employed in the diagnosis of colonisation, our results are highly significant despite the fact that only 3 of 17 subjects became colonised during the 3-day study period. Prolongation of the study beyond 3 days would probably have increased the number of subjects colonised. However, it is extremely difficult for normal subjects to sustain this abnormal voiding pattern, and there is of course the possibility of producing a urinary tract infection.

Introital and urethral colonisation with pathogens is but one of many factors that have been implicated in producing susceptibility to lower urinary tract infection. Some of these conditions are considered to produce susceptibility by causing reflux of urethral bacterial flora into the bladder (Hinman, 1966). Clearly for such a mechanism to produce infection, urethral pathogens must be present. Table VII lists those factors considered important in producing susceptibility to infection.

Our finding that frequency of micturition may produce introital colonisation allows us to construct a simple picture of the pathogenesis of lower tract infections (Fig. 2). Many of the factors are associated with frequency of micturition and therefore possible introital colonisation. For example, one can now understand how an uninhibited neurogenic bladder could lead to infection, without implicating bladder wall ischaemia and a haematogenous route of invasion as previously suggested (Lapides, 1965). When urinary tract infection is present, the accompanying frequency would ensure the maintenance of the colonised state and provide a source of pathogens for relapse and reinfection.

Summary

Introital swabbing was performed on each of 20 premenopausal female volunteers over a 5-day period, 2 swabs being collected each day. During the last 3 days of the 5-day period the volunteers were requested to void every 2 hours.

Analysis of our data shows:

1. Perineal bacterial flora varies in number and type of organisms from hour to hour and day day.
2. Quantitative culturing is of little help in distinguishing colonisation of the introitus with urinary pathogens from mere intermittent contamination of the introitus with the same pathogens.
3. Our results suggest that 4 or more consecutive isolates of the potential urinary pathogens from the introitus over a 48-hour period signify colonisation.
4. Frequency of micturition increases the risk of colonisation of the introitus with potential urinary pathogens.

The significance of these findings is discussed, in relation to the previous work of other investigators.

References

BAILEY, R. R., GOWER, P. E., ROBERTS, A. P. and STACEY, G. (1973). Urinary-tract infection in non-pregnant women. *Lancet*, **2**, 275-277.

BROOKS, D. and MAUDAR, A. (1972). Pathogenesis of the urethral syndrome in women and its diagnosis in general practice. *Lancet*, **2**, 896-898.

BRUCE, A. W., CHADWICK, P., HASSAN, A. and VANCOTT, G. F. (1973). Recurrent urethritis in women. *Canadian Medical Association Journal*, **108**, 973-976.

DIERAUF, L. A., GOWDEY, A. C. and GRANT MULHOLLAND, S. (1974). Bacterial invasion of the urinary tract by way of the vaginal route in the rat. *Surgery, Gynecology and Obstetrics*, **138**, 62-64.

ELKINS, I. B. and COX, C. E. (1974). Perineal, vaginal and urethral bacteriology of young women. 1. Incidence of gram-negative colonization. *Journal of Urology*, **111**, 88-92.

GLEASON, F. (1971). *The Case against the Clean Catch*. (Eaton film library.)

HINMAN, F. (1966). Mechanisms for the entry of bacteria and the establishment of urinary infection in female children. *Journal of Urology*, **96**, 546-550.

LAPIDES, J. (1965). The role of hydrostatic pressure and distension in urinary tract infection. In *Progress in Pyelonephritis*. Ed. by E. H. Kass. Philadelphia, Davis, pp. 578-580.

MARSH, F. P., MURRAY, M. and PANCHAMIA, P. (1972). The relationship between bacterial cultures of the vaginal introitus and urinary infection. *British Journal of Urology*, **44**, 368-375.

MOTZKIN, D. (1972). The bacteriological diagnosis and treatment of urinary tract infection. *Journal of Urology*, **107**, 454-457.

O'GRADY, F. W., RICHARDS, B., MCSHERRY, M. A., O'FARRELL, S. M. and CATTELL, W. R. (1970). Introital enterobacteria, urinary infection and the urethral syndrome. *Lancet*, **2**, 1208-1210.

STAMEY, T. A. (1973). The role of introital enterobacteria in recurrent urinary infections. *Journal of Urology*, **109**, 467-472.

The Authors

John M. Seddon, FRCS (C) Chief Resident, Department of Urology.
Andrew W. Bruce, FRCSE, FRCS (C), FACS, Professor and Chairman, Department of Urology.
Paul Chadwick, MB, BSc, Dip. Bact. (Lond.), Professor and Chairman, Departmeut of Bacteriology.
Donna Carter, RN. Assistant Head Nurse, Nursing Department, Kingston General Hospital, Kingston.

Correspondence to: John M. Sedden, Department of Urology, Queen's University, Kingston, Ontario, Canada.

British Journal of Urology (1976), **48**, 219–220 ©

Short Case Report

Localised Primary Amyloidosis of the Bladder

The urinary bladder is rarely the site of primary amyloidosis. In 1961, Kinzel, Harrison and Utz reviewed the world literature and reported on 16 cases, adding 5 of their own. Since that time, 17 additional cases have been reported and intravenous pyelography has been normal in all of these 38 cases.

We have recently seen and treated 2 patients with primary bladder amyloidosis and associated ureteric obstruction.

Case Reports

Case 1

A 70-year-old female presented with a 1-year history of haematuria, dysuria and suprapubic pressure. Initial pyelograms showed minimal right ureteric obstruction (Fig. 1). A cystoscopic examination revealed the floor of the bladder and the right lateral wall to be replaced by a flat, sessile mass covered by oedematous mucosa which was resected and fulgurated. Histologically, the specimen showed large aggregates of amyloid material and the absence of any carcinoma (Fig. 2). At follow-up examination, 6 months later, she was free of symptoms.

Case 2

A 71-year-old female presented with recurrent urinary tract infections, dysuria, frequency and haematuria. After an initial pyelogram showed only mild left caliectasis, cystoscopy revealed scattered areas of reddened mucosa and a biopsy showed only chronic cystitis. She was placed on suppressive antibiotics but a follow-up pyelogram 9 months later revealed severe left and a moderate right upper tract dilatation (Fig. 3).

Repeat cystoscopy showed the entire trigone to be involved with a diffuse, haemorrhagic mass involving both ureteric orifices. A biopsy showed diffuse amyloidosis.

Because of her worsening symptoms and progressive ureteric involvement, the urine was diverted into an ileal segment. 6 months following surgery her collecting systems had returned to normal.

Comment

The localised deposition of amyloid has been reported in diverse sites, including the respiratory tract, skin and heart. Relevant to the genito-urinary system, involvement of the kidney, ureters, seminal vesicles, prostate, penis and testes has been noted by Nagel (1966).

All of the previously reported 38 cases had normal pyelograms. Our 2 cases appear unique in that both patients had ureteric obstruction.

Cystoscopically, the lesion resembles a sessile neoplasm with mucosal oedema. The clinical diagnosis of amyloidosis is impossible, making biopsy mandatory.

Various modalities of treatment have been employed, including transurethral biopsy and resection, partial cystectomy, radium implantation and urinary diversion. The only previous ileal urinary diversions performed for

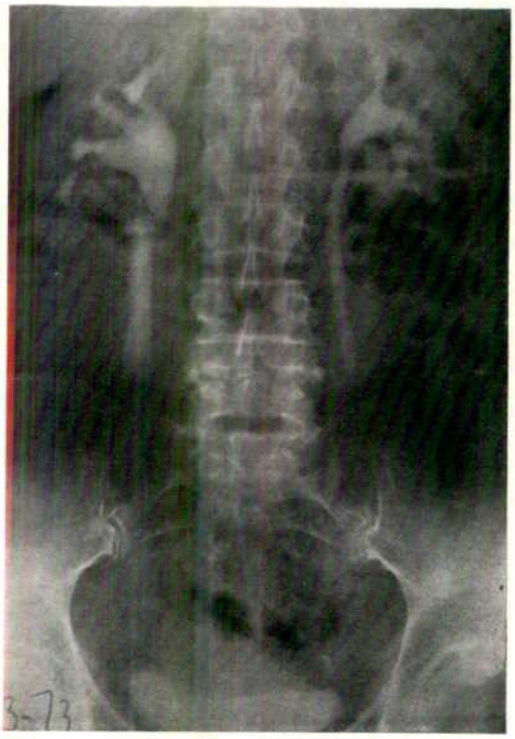


Fig. 1. Case 1. Intravenous pyelogram showing right ureteric dilation.

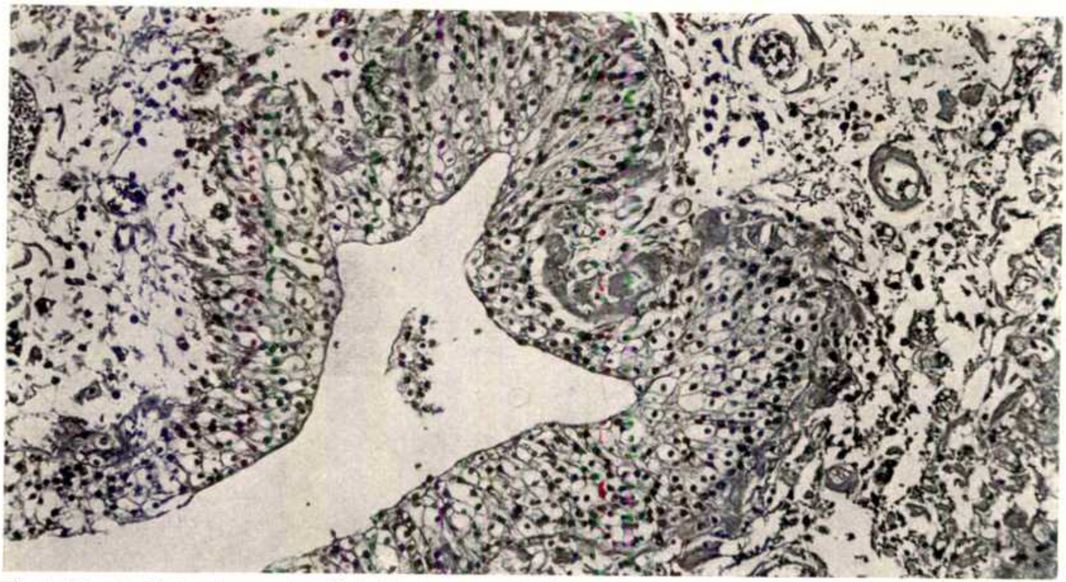


Fig. 2. Case 1. Photomicrography of bladder mucosa and submucosa. Note amyloid deposition immediately beneath mucosa (× 150).

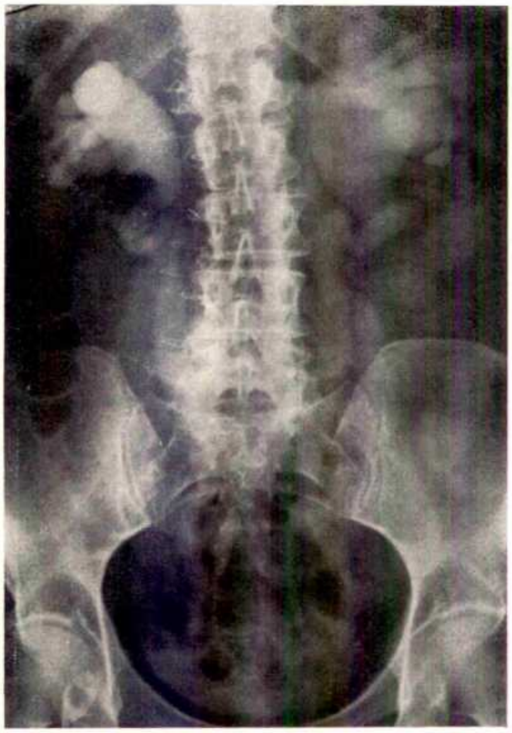


Fig. 3. Case 2. IVP. Bilateral upper tract dilatation.

amyloidosis of the bladder were done by Hudson and Tingley (1965) and by Kinzel *et al.* (1961), both for severe irritable bladder symptoms. We performed an ileal diversion because of progressive bilateral ureteric obstruction.

Read at South Central Section Meeting, A.U.A., Denver, Colorado, September 1974.

RICHARD A. BLATH and JAMES G. BUCY
Washington University School of Medicine, Genitourinary Division, Department of Surgery, St Louis, Missouri 63110, USA

References

HUDSON, H. C. and TINGLEY, J. O. (1965). Primary amyloidosis of the bladder. *Journal of the Medical Association of Alabama*, **35**, 353-355.

KINZEL, R. C., HARRISON, E. G. and UTZ, D. C. (1961). Primary localized amyloidosis of the bladder. *Journal of Urology*, **85**, 785-795.

NAGEL, R. (1966). Localized amyloidosis of the bladder. *Journal of Urology*, **88**, 56-59.

CURRENT UROLOGICAL LITERATURE: SELECT BIBLIOGRAPHY[1]

The List of Current Urological Literature is now arranged to correspond to the order in which papers are published in the *Journal*, *i.e.*, in anatomical order beginning with papers on the kidney.

A general selection is included at the end

KIDNEY

General. Radiolucent filling defects of renal pelvis: classification and report of unusual cases. (R. S. Malek *et al.*) *J. Urol.* 1975, **114**, 508.

Aberrant renal papilla: diagnostic dilemma. (A. E. Feldman *et al.*) *J. Urol.* 1975, **114**, 144.

Chronic pseudocystic urinary extravasation. (F. Schreiter *et al.*) *Aktuel. Urol.* 1975, **6**, 157.

Spontaneous urinary extravasation. (J. M. Beal.) *Ill. Med. J.* 1975, **148**, 165.

Malakoplakia of kidney and bladder with large bowel invasion. (A. J. Clarke *et al.*) *Br. J. Urol.* 1975, **47**, 376.

Effects of anesthetics on kidney. (S. Deutsch.) *Surg. Clin. North Am.* 1975, **55**, 775.

In vitro studies on human renal calices. (N. Longrigg.) *J. Urol.* 1975, **114**, 325.

Regeneration of the renal calyces after calycectomy. An experimental study. (W. Lutzeyer *et al.*) *Eur. Urol.* 1975, **1**, 198.

Changes in the upper urinary tract as demonstrated on intravenous pyelography and micturating cystourethrography in patients with spinal cord injury. (A. T. Scher.) *Paraplegia*, 1975, **13**, 157.

Congenital Anomalies. Congenital arteriovenous fistulas: report of case and review of literature. (J. P. Neifeld *et al.*) *J. Urol.* 1975, **114**, 648.

Complicated pyelo-ureteral duplication in the adult. Report of 23 cases. (H. J. Naulleau *et al.*) *Ann. Urol.* 1975, **9**, 123.

Dysplastic kidney with duplicated bladder and ureters. (M. H. Antar.) *J. Fla. Med. Assoc.* 1975, **62**, 51.

Intrathoracic kidney. (R. H. Lozano and C. Rodriguez.) *J. Urol.* 1975, **114**, 601.

Spectrum of renal tubular ectasia and hepatic fibrosis. (R. Six *et al.*) *Radiology*, 1975, **117**, 117.

Familial occurrence of hydronephrosis and of mega-ureter-megacystis syndrome. (H. Grobe and L. Diekmann.) *Fortschr. Geb. Röntgenstr. Nuklearmed.* 1975, **123**, 116.

Congenital arterio-venous aneurysms of the kidney: with reference to 3 cases. (J. L. Brunier *et al.*) *Ann. Radiol.* 1975, **18**, 559.

Massive unilateral non-functioning hydronephrosis in horseshoe kidney. (L. Love and D. Wasserman.) *Clin. Radiol.* 1975, **26**, 409.

Horseshoe kidney in children. A description of 58 cases. (Y. Soulier and J. Cendron.) *Ann. Chir. Infant* 1975, **16**, 325.

Partial thoracic renal ectopy. (W. Bischoff *et al.*) *Roentgenblatter*, 1975, **28**, 333.

Solitary crossed renal ectopia. (M. M. H. Shah.) *Br. J. Urol.* 1975, **47**, 512.

Fetal renal malformation following treatment of Hodgkin's disease during pregnancy. (M. T. Mennuti *et al.*) *Obstet. Gynecol.* 1975, **46**, 194.

Duplex kidneys: correlation of renal dysplasia with position of ureteral orifice. (G. G. Mackie and F. D. Stephens.) *J. Urol.* 1975, **114**, 274.

Trauma. On the noxious character of organized traumatic perirenal hematoma and prevention of the latter. (C. Dimopoulos *et al.*) *Ann. Urol.* 1975, **9**, 57.

Intraperitoneal rupture of pyonephrosis. (S. U. Rahman.) *Br. J. Urol.* 1975, **47**, 488.

Survival in one case of lesion of the vena cava with division of the vascular pedicle of the right kidney in a closed injury of the abdomen. (R. Banchieri *et al.*) *J. Urol. Néphrol.* 1975, **81**, 609.

Post-traumatic haemoglobinuria. (J. E. Gottesman and J. R. Orecklin.) *Br. J. Urol.* 1975, **47**, 362.

Renal trauma in multiple injured patient. (A. S. Cass.) *J. Urol.* 1975, **114**, 495.

Control of experimental traumatic renal hemorrhage by embolization with autogenous blood clot. (V. P. Chuang *et al.*) *Radiology*, 1975, **117**, 55.

Traumatic kidney rupture in hydronephrosis. (D. Jonas *et al.*) *Urol. Res.* 1975, **3**, 91.

Occupational damages of kidney. (V. Lachnit.) *Arbeitsmed. Sozialmed. Präventivmed.* 1975, **10**, 160.

Spontaneous rupture of kidney with perirenal hematoma. (W. S. McDougal *et al.*) *J. Urol.* 1975, **114**, 181.

Spontaneous rupture of the renal collecting system. (G. Höltl and P. P. Figdor.) *Int. Urol. Nephrol.* 1975, 7, 109.

Delayed flank approach to isolated renal trauma in children. (H. W. Schoenberg and J. G. Gregory.) *J. Pediatr. Surg.* 1975, **10**, 525.

Renal trauma during laparotomy for intra-abdominal injury. (A. S. Cass.) *Arch. Surg.* 1975, **110**, 950.

Fistula. Congenital arteriovenous fistulas of the kidney. (B. Becq-Giraudon and Y. Sudre.) *Ouest Méd.* 1975, **28**, 1465.

Arteriovenous fistula of renal vessels: surgical management. (K. B. Cummings *et al.*) *J. Urol.* 1975, **114**, 776.

Renal arteriovenous fistula treated by endo-fistulorrhaphy. (R. M. Ehrlich.) *Arch. Surg.* 1975, **110**, 1195.

Malignant renal arteriovenous fistulae: a cause of reversible cardiac failure. (E. M. Bass and M. H. Lipper.) *S. Afr. Med. J.* 1975, **49**, 1361.

Infections. Long term results of conservative surgery for bilateral renal tuberculosis. (M. S. Stoica.) *J. Urol. Néphrol.* 1975, **81**, 515.

Angiography and renal tuberculosis. (M. Haertel and A. Jonutis.) *Roentgenblaetter*, 1975, **28**, 511.

Conservative treatment of renal tuberculosis. (N. W. Horne and W. S. Tulloch.) *Br. J. Urol.* 1975, **47**, 481.

Destructive forms of renal tuberculosis. (S. Petković *et al.*) *Eur. Urol.* 1975, **1**, 81.

Reactivation of genito-urinary tuberculosis. A retrospective review of 838 cases. (M. R. Butler and J. D. O'Flynn.) *Eur. Urol.* 1975, **1**, 14.

Cavernotomy in renal tuberculosis. (A. Steinbock.) *Ann. Chir. Gynaecol. Fenn.* 1975, **64**, 203.

---

[1] Titles in this list have been taken from those listed in *Current Contents: Clinical Practice* published by Institute for Scientific Information, Philadelphia

Ethambutol regimen in renal tuberculosis. (H. Wechster.) *J. Urol.* 1975, **114**, 498.

Renal tuberculosis. (N. W. Horne.) *Brit. J. Hosp. Med.* 1975, **14**, 158.

Bacteriuria in patients with spinal cord lesions. (E. Newman and M. Price.) *J. Am. Med. Wom. Assoc.* 1975, **30**, 403.

Bacteriuria, reflux and renal scarring. (J. M. Smellie and I. C. S. Normand.) *Arch. Dis. Child.* 1975, **50**, 581.

The microbial flora of the vagina and its relationship to bacteriuria in diabetic and non-diabetic women. (D. N. Williams *et al.*) *Br. J. Urol.* 1975, **47**, 453.

Long-term therapy for chronic bacteriuria in men. (R. B. Freeman *et al.*) *Ann. Intern. Med.* 1975, **83**, 133.

Rapid miniaturized tests for bacteriuria microstix and bacturcult urine tests. (C. C. Winter.) *J. Urol.* 1975, **114**, 755.

Methicillin induced interstitial nephritis. (B. Zacherle.) *J. West. Med.* 1975, **123**, 380.

Acute adult onset bacterial nephritis: long-term urographic and angiographic followup. (R. M. Lilienfeld and A. Lande.) *J. Urol.* 1975, **114**, 14.

Immunogenicity of *Escherichia coli* O antigen in upper urinary tract infection. (J. A. Whitworth *et al.*) *Kidney Int.* 1975, **8**, 316.

Some principles underlying the prophylaxis and therapy of acute inflammatory affections of the kidneys. (M. N. Zilberman *et al.*) *Sov. Med.* 1975, no. 7, July, 77.

Urinary lactic dehydrogenase isoenzyme 5 in the differential diagnosis of kidney and bladder infection. (H. F. Carvajal *et al.*) *Kidney Int.* 1975, **8**, 176.

Chronic renal abscess. (A. Rabin *et al.*) *Gaz. Med. Fr.* 1975, **82**, 4037.

Virus infections and kidney disease. (R. J. Howard and H. H. Balfour.) *Minn. Med.* 1975, **58**, 809.

Influence of oestrogen on experimental pyelonephritis caused by *Escherichia coli.* (E. Harle *et al.*) *Lancet*, 1975, **2**, 283.

Urinary white cell excretion rate in patients with chronic pyelonephritis. (G. E. Baltzer *et al.*) *Med. Welt.* 1975, **26**, 1652.

Medical and surgical aspects of pyelonephritis in childhood. (J. R. Soriano *et al.*) *An. Esp. Pediatr.* 1975, **8**, suppl. 3.1.

Urographic diagnosis of pyelonephritis under consideration of clinical parameters. (N. Hasse and F. Schwarz.) *Radiol. Diagn.* 1975, **16**, 375.

Nitrofurantoin, sulfamethiazole and cephalexin urinary concentration in unequally functioning pyelonephritic kidneys. (J. W. Sullivan *et al.*) *J. Urol.* 1975, **114**, 343.

Emphysematous pyelonephritis: report of 3 cases treated by nephrectomy. (S. R. Dunn *et al.*) *J. Urol.* 1975, **114**, 348.

New thoughts concerning xanthogranulomatous pyelonephritis (X-P). (S. Gammill *et al.*) *Am. J. Roentgen. Radium Ther. Nucl. Med.* 1975, **125**, 154.

Calculi. Selective caliceal catherization for stone manipulation. (T. P. Ball and L. M. Bobroff.) *J. Urol.* 1975, **114**, 172.

Surgical management of symptomatic solitary caliceal calculus. (J. F. Redman *et al.*) *J. Urol.* 1975, **114**, 175.

100 cases of nephrolithotomy under hypothermia. (J. E. A. Wickham *et al.*) *Eur. Urol.* 1975, **1**, 71.

The immunological integrity of matrix substance A and its possible detection and quantitation in urine. (S. Moore and G. Gowland.) *Br. J. Urol.* 1975, **47**, 489.

Riddle of Randall's plaques. (E. L. Prien.) *J. Urol.* 1975, **114**, 500.

Epidemiology of renal stones in a middle-aged male population. (S. Ljunghall and H. Hedstrand.) *Acta Med. Scand.* 1975, **197**, 439.

The fate of the remaining kidney following nephrectomy for kidney stones. (R. Küss *et al.*) *Ann. Urol.* 1975, **9**, 51.

Electron microscopic studies on the mechanism of renal stone formation with special reference to changes in the proximal tubular lumen. (T. Kawada *et al.*) *Jpn. J. Urol.* 1975, **66**, 455.

Renal stones structure in primary hyperparathyroidism. (L. Cifuentes Delatte *et al.*) *Rev. Clin. Esp.* 1975, **138**, 305.

Kidney stones: clinical problem. (M. B. Block.) *Ariz. Med.* 1975, **32**, 727.

Furosemide, inductothermy and sinusoidal modulated currents in the treatment of patients with urolithiasis. (G. O. Chumak and V. F. Chalaya.) *Sov. Med.* 1975, no. 7, July, 134.

Leukonychia totalis, multiple sebaceous cysts and renal calculi. (L. L. Bushkell and R. J. Gorlin.) *Arch. Dermatol.* 1975, **111**, 899.

Recurrent renal calculi—need for adequate work-up. (W. Shieber.) *Surgery*, 1975, **78**, 126.

Composition of renal calculi in Hungary. (M. Berenyi.) *Acta Chir. Acad. Sci. Hung.* 1975, **16**, 73.

The influence of calcium content of water, intake of vegetables and fruit and of other foods factors upon the incidence of renal calculi. (G. A. Rose and E. J. Westbury. *Urol. Res.* 1975, **3**, 61.

Acetazolamide-induced renal calculi. (M. A. Rubenstein and J. C. Bucy.) *J. Urol.* 1975, **114**, 610.

Renal suffering caused by lithiasis. (J. L. G. Chillon *et al.*) *Cir. Esp.* 1975, **29**, 83.

Circulatory Disorders. Arteriovenous malformation: value of renal angiography for filling defect in renal pelvis. (J. B. Po *et al.*) *J. Urol.* 1975, **114**, 607.

Variations of origin of the renal artery. A review covering 403 aortographies. (J. Aubert and K. Koumare.) *Eur. Urol.* 1975, **1**, 182.

Renal artery dissection—complication of catheter arteriography. (L. B. Talner *et al.*) *Radiology*, 1975, **117**, 291.

Ex vivo renal artery reconstruction. (F. O. Belzer *et al.*) *Ann. Surg.* 1975, **182**, 456.

Aneurysmal changes of renal arteries in angiogram. (H. Keller *et al.*) *Roentgenblaetter*, 1975, **28**, 327.

Direct vasoconstrictor effect of mannitol on renal artery. (S. P. Temes *et al.*) *Surg. Gynecol. Obstet.* 1975, **141**, 223.

Phaeochromocytoma with renal artery stenosis and high plasma renin activity. (M. Ishibashi *et al.*) *Jpn. Heart J.* 1975, **16**, 741.

Renal artery stenosis—then and now. (R. Birchall and J. Birchall.) *South. Med. J.* 1975, **68**, 1109.

Renal artery stenosis—complication of needle puncture for manometry—case of subintimal dissection with spontaneous resolution. (J. J. Kaufman.) *Am. J. Surg.* 1975, **130**, 347.

Post-traumatic renal artery stenosis—cure of hypertension by late revascularisation. (T. A. Depner *et al.*) *Arch. Surg.* 1975, **110**, 1150.

Renal artery aneurysms: significance of macroaneurysms exclusive of dissections and fibrodysplastic mural dilations. (J. C. Stanley *et al.*) *Arch. Surg.* 1975, **110**, 1327.

Aneurysm of a polar renal artery. (F. Cifarelli *et al.*) *Surgery*, 1975, **78**, 660.

Aneurysm of the renal artery with a case of extracorporeal repair. (H. Gaylis and I. Lissoos.) *S. Afr. Med. J.* 1975, **49**, 1963.

Indications for surgery on renal artery aneurysms. (J. P. McCarron *et al.*) *J. Urol.* 1975, **114**, 177.

Acute renal artery occlusion. (C. U. McRae.) *N.Z. Med. J.* 1975, **82**, 344.

Retrograde renal phlebography with balloon occlusion of renal artery—technique and scope of a new method. (M. Georgi *et al.*) *Fortschr. Geb. Roentgenstr. Nuklearmed.* 1975, **123**, 341.

Multiple aneurysms in a child. (J. L. Williams.) *Proc. R. Soc. Med.* 1975, **68**, 523.

Frequency of the retroaortic left renal vein in adults. (G. P. Schmidt and M. Loeweneck.) *Urol. Int.* 1975, **30**, 332.

Unilateral renal vein thrombosis during mid-childhood. Progress in recognition and management. (A. L. Florman *et al.*) *Clin. Pediatr.* 1975, **14**, 734.

Small atrophic kidney secondary to renal vein thrombosis: report of case diagnosed arteriographically. (R. E. Clark *et al.*) *J. Urol.* 1975, **114**, 457.

Thrombosis of the renal vein and vena cava. (F. C. Luft *et al.*) *J.A.M.A.* 1975, **234**, 1158.

Radiologic diagnosis of thrombosis of renal veins. (F. Wiedner and G. Schwarz.) *Roentgenblaetter*, 1975, **28**, 518.

Renovascular hypertension secondary to arterial fibrodysplasia in adults—criteria for operation and results of surgical therapy. (J. C. Stanley and W. J. Fry.) *Arch. Surg.* 1975, **110**, 922.

On the use of renal angiography and intravenous urography in the investigation of renovascular hypertension. (U. Erikson *et al.*) *Acta Med. Scand.* 1975, **198**, 39.

Recognition and management of renovascular hypertension. (J. H. Foster and J. A. Oates.) *Hosp. Pract.* 1975, **10**, 61.

Operative management of renovascular hypertension. (H. D. Berkowitz *et al.*) *Pa. Med.* 1975, **78**, 47.

Surgical treatment of renovascular hypertension in children. (R. J. Stoney *et al.*) *J. Pediatr. Surg.* 1975, **10**, 631.

Renovascular hypertension in renal tuberculosis. (H. M. Pinedo and S. A. Duursma.) *Neth. J. Med.* 1975, **18**, 184.

Renovascular hypertension. Diagnosis and treatment. (M. G. Eguaras *et al.*) *Rev. Clin. Esp.* 1975, **138**, 515.

Renovascular hypertension: role of urologist. (W. R. Fair.) *J. Urol.* 1975, **114**, 655.

Extracorporeal repair of the renal artery for renovascular hypertension. A case report. (J. A. Martinez-Piñero and M. G. Martin.) *Eur. Urol.* 1975, **1**, 165.

Acute hypertension and perirenal haematoma—a new aspect of Page's syndrome. (G. Lindgårdh and J. Schönebeck.) *Br. J. Urol.* 1975, **47**, 359.

Hypertension and unilateral parenchymal renal disease. (E. D. Vaughan *et al.*) *J.A.M.A.* 1975, **233**, 1177.

Iatrogenic renal hypertension. (H. B. Eckstein and R. J. Fitzgerald.) *Aktuel. Urol.* 1975, **6**, 185.

Segmentary renal hypoplasia and arterial hypertension. (R. V. Navarrete *et al.*) *Rev. Clin. Esp.* 1975, **139**, 81.

Postoperative improvement of hypertension in primary aldosteronism and Cushing's syndrome. (Y. Aso and K. Kinoshita.) *Urol. Int.* 1975, **30**, 386.

Cysts. A case of adrenal pseudocyst. (J. M. Nys *et al.*) *Acta Urol. Belg.* 1975, **43**, 295.

Pseudocysts of kidney, with report of hemorrhagic pararenal pseudocyst associated with multiple small renal infarcts. (L. Rubin.) *J. Urol.* 1975, **114**, 603.

Solitary renal cyst. (A. Joannard *et al.*) *Pediatrie*, 1975, **30**, 629.

Effect of intracystic pantopaque on renal cysts. (M. M. Raskin *et al.*) *J. Urol.* 1975, **114**, 678.

Spontaneous peripelvic urinary extravasation secondary to benign renal cyst. (G. J. Gavrell and G. A. LeBlanc.) *J. Urol.* 1975, **114**, 617.

Needling renal cysts and tumours: cytology and radiology. (T. Sherwood and P. A. Trott.) *Br. Med. J.* 1975, **3**, 755.

Percutaneous renal cyst puncture: unusual results in 2 cases. (H. J. Mindell.) *J. Urol.* 1975, **114**, 332.

Segmental multicystic renal dysplasia. (T. G. Daughtridge.) *J. Can. Assoc. Radiol.* 1975, **26**, 149.

Spontaneous remission of peripelvic renal cysts. (J. F. Steel *et al.*) *J. Urol.* 1975, **114**, 10.

Conservative surgical treatment of a kidney hydatid cyst. (J. Lemans and A. Kotowicz.) *Acta Urol. Belg.* 1975, **43**, 257.

Neoplasms. Permanent stop of renal circulation by embolisation with microspheres—preliminary report. (K. Barth *et al.*) *Urologe*, 1975, **14**, 250.

Occlusion of the renal artery by intrarenal injection of thrombin in a case of inoperable renal tumour. (M. Georgi *et al.*) *Dtsch. Med. Wochenschr.* 1975, **100**, 2428.

Balloon occlusion of renal artery in tumor nephrectomy. (M. Marberger and M. Georgi.) *J. Urol.* 1975, **114**, 360.

Elective transcatheter renal artery occlusion prior to nephrectomy. (Y. Ben-Menachem *et al.*) *J. Urol.* 1975, **114**, 355.

Regression of a renal-cell metastatic osseous lesion following treatment. (W. Dorn and P. Gladden.) *J. Bone Joint. Surg.* [*Am.*], 1975, **57**, 869.

Regression of a renal-cell metastatic osseous lesion following treatment. (W. Dorn *et al.*) *J. Bone Joint Surg.* [*Br.*] 1975, **57**, 869.

Stauffer's syndrome—diagnostic help in hypernephroma. (G. H. Jacobi and Th. Philipp.) *Clin. Nephrol.* 1975, **4**, 113.

Cancer of the kidney. (P. C. Peters.) *Tex. Med.* 1975, **71**, 69.

Agranulocytosis in the hypernephroid cancer of the kidney. (V. L. Melnikov *et al.*) *Sov. Med.* 1975, no. 7, July, 135.

Bilateral cancer of the kidney. (D. Lange and J. Lange.) *J. Urol. Néphrol.* 1975, **81**, 523.

Results of extensive nephrectomy with ganglionic curage in primitive cancer of adult kidney. (J. Cukier *et al.*) *J. Urol. Néphrol.* 1974, **80**, 465.

New technique for selective occlusion of kidney using silicone suspension containing iron directed by external electromagnet—application to case of renal cancer. (R. D. Turner *et al.*) *J. Urol. Néphrol.* 1974, **80**, 477.

Hormones in treatment of metastatic renal cancer. (A. Morales *et al.*) *J. Urol.* 1975, **114**, 692.

Renal cancer to-day—suspicion, diagnosis or therapy? (E. Schumann *et al.*) *Radiol. Clin.* 1975, **44**, 377.

A too often overlooked disease: cancer of the kidney. (J. Aubert and J. Casamayou.) *Ouest Med.* 1975, **28**, 1425.

Treatment of cancer of the kidney. (D. Grasset.) *Praxis*, 1975, **64**, 1540.

Contribution to the optimization of telecobalt irradiation of malignant renal tumours. (F. Lehmann *et al.*) *Radiobiol. Radiother.* 1975, **15**, 259.

Metastatic tumors to the kidney. (W. B. Stroughton and D. F. Milam.) *W. Va. Med. J.* 1975, **71**, 199.

Importance of renovasographic examination method in renal tumour diagnosis. (E. Banzhaf *et al.*) *Radiol. Diagn.* 1975, **16**, 235.

Renal tumor after pyelography with thorotrast. (G. Fransen *et al.*) *Acta Urol. Belg.* 1975, **43**, 268.

Management of benign renal tumors of infancy—case report of a congenital mesoblastic nephroma (leiomyomatous harmatoma). (A. Eidelman *et al.*) *Helv. Paediatr. Acta*, 1975, **30**, 169.

Arteriovenous shunting in renal pelvic tumors. (W. H. Forman *et al.*) *South. Med. J.* 1975, **68**, 992.

Examinations of dose distribution for the irradiation of malignant renal tumours with ultrahard bremsstrahlung from a 28 mev betatron by 3 stationary fields. (M. Stecher *et al.*) *Radiobiol. Radiother.* 1975, **16**, 279.

Percutaneous catheter-aided infarction of renal tumors: preliminary report. (S. B. Paster *et al.*) *J. Urol.* 1975, **114**, 351.

Treatment of bilateral synchronous renal pelvic tumors with bench surgery. (M. G. McLoughlin.) *J. Urol.* 1975, **114**, 463.

Renal tumor—collective study. (Klippel.) *Aktuel Urol.* 1975, **6**, 175.

Tumour of the excretory duct of the remaining kidney after nephrectomy for Grawitz' tumour. Conservative treatment. (G. Raymond *et al.*) *J. Urol. Néphrol.* 1975, **82**, 619.

Radiology and fine needle aspiration biopsy in the diagnosis of tumours of the kidney. (J. Edgren *et al.*) *Ann. Chir. Gynaecol. Fenn.* 1975, **64**, 209.

Mesenteric vascularisation of malignant renal tumours. (M. Haertel and R. Kunz.) *Fortschr. Geb. Roentgenstr. Nuklearmed.* 1975, **123**, 338.

Interesting case—ex-vivo renal tumor resection and subsequent autotransplantation. (P. H. Petritsch *et al.*) *Aktuel. Urol.* 1975, **6**, 253.

Angiography of malignant adrenal tumours. (M. Georgi *et al.*) *Aktuel. Urol.* 1975, **6**, 227.

The diagnosis of renal pseudotumours. (A. T. Carty *et al.*) *Br. J. Urol.* 1975, **47**, 495.

Renal sarcoma in neonates. (H. J. Buhr *et al.*) *Klin. Pädiatr.* 1975, **187**, 361.

Angiomyolipoma of kidney. (B. N. Rao and P. V. B. Rao.) *Clinician*, 1975, **39**, 277.

Spontaneous rupture of an angiomyolipoma of the kidney. (S. Wapnick *et al.*) *Int. Surg.* 1975, **60**, 485.

Fetal mesenchymal hamartoma of kidney—tumor of secondary mesenchyme. (H. J. Wigger.) *Cancer*, 1975, **36**, 1002.

Studies on immune status of patients with renal adenocarcinoma. (S. Brosman *et al.*) *J. Urol.* 1975, **114**, 375.

Combined intra-arterial actinomycin D and radiation therapy for surgically unresectable hypernephroma. (A. L. Wiley *et al.*) *J. Urol.* 1975, **114**, 198.

Study of cellular immunity in the course of nephro-epithelioma. Preliminary study concerning 12 cases. (D. Lange and Y. du Pasquier.) *J. Urol. Néphrol.* 1975, **81**, 543.

Giant retroperitoneal liposarcoma in the vicinity of the right kidney. (A. M. Dajani.) *Int. Surg.* 1975, **60**, 489.

Renal localisation of lymphosarcoma in the child. (T. J. Sutton *et al.*) *J. Radiol. Electrol.* 1975, **56**, 685.

Hypernephroma with polycythaemia: a post-operative complication. (N. Menzies-Gow.) *Br. J. Urol.* 1975, **47**, 499.

Declining mortality and improving survival from Wilms' tumor. (R. B. Everson.) *Med. Pediatr. Oncol.* 1975, **1**, 3.

Experience with thoraco-abdominal incision for nephroblastoma in children less than 3 years old. (A. T. Cole and F. A. Fried.) *J. Urol.* 1975, **114**, 114.

Wilms' tumor in the crossed ectopic kidney. (M. Berant *et al.*) *J. Pediatr. Surg.* 1975, **10**, 555.

Leukemia in children with Wilms tumor, (A. D. Schwartz *et al.*) *J. Pediatr.* 1975, **87**, 374.

Bilateral Wilms' tumour. (J. Bond.) *Lancet*, 1975, **2**, 482.

Echocardiographic diagnosis of right atrial extension of Wilms' tumor. (Z.Q. Farooki *et al.*) *Am. J. Cardiol.* 1975, **36**, 363.

Changing concepts in the management of Wilms's tumour and rhabdomyosarcoma. (J. E. Freeman.) *Proc. R. Soc. Med.* 1975, **68**, 660.

Successful treatment of Wilms tumor with intracranial metastases. (D. Traggis *et al.*) *Pediatrics*, 1975, **56**, 472.

Wilms tumor—histologic variation and prognosis. (W. Lawler *et al.*) *Cancer*, 1975, **36**, 1122.

Hepato-toxicity of chemotherapy following nephrectomy and radiation therapy for right-sided Wilms tumor. (P. Mcveagh and H. Ekert.) *J. Pediatr.* 1975, **87**, 627.

Adriamycin cardiotoxicity in a child with Wilms tumor—report of a case and review of literature. (M. A. Gerber *et al.*) *J. Pediatr.* 1975, **87**, 629.

Su un caso di tumore di Wilms bilaterale. (P. Balossi *et al.*) *Minerva Pediatr.* 1975, **27**, 1683.

Can permanent cures following enucleation of tumour in bilateral nephroblastoma be expected. (G. Kaiser *et al.*) *Z. Kinder. Chir. Grenzgeb.* 1975, **17**, 233.

Electrolyte imbalance and cardiac arrest following nephrectomy for Wilms-Tumour. (I. Larsson and L. Okmian.) *Z. Kinder. Chir. Grenzgeb.* 1975, **17**, 238.

Prognosis and treatment of Wilms tumor at Great Ormond Street Hospital for Sick Children, 1960-1972. (J. V. Bond.) *Cancer*, 1975, **36**, 1202.

Wilms tumor in horseshoe kidney. (J. M. Ocanalosa *et al.*) *Rev. Esp. Pediatr.* 1975, **31**, 731.

Familial Wilms's tumor. (A. G. Knudson and L. C. Strong.) *Am. J. Hum. Genet.* 1975, **27**, 809.

Unusual manifestations of metastatic renal cell carcinoma. (C. S. Coffman and M. H. Schreiber.) *Tex. Med.* 1975, **71**, 60.

The angiographic evaluation of renal pelvic carcinoma. (J. J. Pollen *et al.*) *Br. J. Urol.* 1975, **47**, 363.

Elevated prostaglandins and suppressed parathyroid hormone associated with hypercalcemia and renal cell carcinoma. (R. P. Robertson *et al.*) *J. Clin. Endocrinol. Metab.* 1975, **41**, 164.

Secondary carcinomas of kidney. (D. G. Wagle *et al.*) *J. Urol.* 1975, **114**, 30.

Is nephrectomy justified in patients with metastatic renal carcinoma? (D. E. Johnson *et al.*) *J. Urol.* 1975, **114**, 27.

Carcinoma of the renal pelvis: a ten-year review. (J. D. Donnelly and W. W. Koontz.) *South. Med. J.* 1975, **68**, 943.

Arteriovenous fistulae secondary to renal cell carcinoma—clinical and cardiovascular manifestations.—Report of a case. (M. V. Rodgers *et al.*) *Circulation*, 1975, **52**, 345.

A clinical study on renal cell carcinoma. (T. Minami *et al.*) *Jpn. J. Urol.* 1975, **66**, 474.

Renal cell carcinoma: natural history and chemotherapeutic experience. (J. J. Lokich and J. H. Harrison.) *J. Urol.* 1975, **114**, 371.

Place of bone scan in diagnosis of renal cell carcinoma. (A. T. Cole *et al.*) *J. Urol.* 1975, **114**, 364.

Extended angiography in diagnosis and treatment of renal carcinoma. (L. A. Klein and H. Eisenberg.) *J. Urol.* 1975, **114**, 366.

Non-urologic manifestations of renal cell carcinoma. (G. H. Jacobi.) *Aktuel. Urol.* 1975, **6**, 177.

Prolonged survival from renal cell carcinoma after renal allotransplantation. (J. G. Maxwell *et al.*) *J. Urol.* 1975, **114**, 615.

Renal cell carcinoma presenting as systemic hypertension of sudden onset. (V. Lopez-Majano *et al.*) *Int. Surg.* 1975, **60**, 491.

Carcinoma of the kidney and selective renal arteriography. (J. Aubertin *et al.*) *J. Urol. Néphrol.* 1975, **81**, 598.

The diagnosis of transitional cell carcinoma of the renal pelvis. (P. J. P. van Blerk and E. Levine.) *S. Afr. J. Surg.* 1975, **13**, 169.

Regression of renal carcinoma following radiation therapy. (R. B. Malkin.) *J. Urol.* 1975, **114**, 782.

Analysis of factors affecting survival in 150 patients with renal carcinoma. (I. M. Thompson *et al.*) *J. Urol.* 1975, **114**, 694.

Clear-cell carcinoma of the kidney. Treatment with a precise technique using cobalt-60. (Y. Horn *et al.*) *Radiol. Clin.* 1975, **44**, 470.

Bony metastasis in renal cell carcinoma. (S. A. Cook *et al.*) *Cleve. Clin. Q.* 1975, **42**, 263.

Management of metastatic renal carcinoma surgical aspects. (G. D. Chisholm.) *Proc. R. Soc. Med.* 1975, **68**, 775.

Tumour-associated antibodies against renal cell carcinomas detected by immunofluorescence. (R. Ackermann.) *Eur. Urol.* 1975, **1**, 154.

Cystadenoma of the kidney in childhood. Five case reports. (C. Nezelof *et al.*) *Arch. Fr. Pédiatr.* 1975, **32**, 815.

Mucinous adenocarcinoma of renal pelvis: discussion of possible pathogenesis. (B. H. Liwniez *et al.*) *J. Urol.* 1975, **114**, 306.

Nephroepithelioma in children expressed by recurring isolated hematuria. Diagnostic problems in 3 cases. (M. Hermier *et al.*) *Arch. Fr. Pédiatr.* 1975, **32**, 709.

Mechanical Disorders. Value of radioisotope renography in follow-up of patients operated upon for hydronephrosis. (K. J. Tveter *et al.*) *J. Urol.* 1975, **114**, 680.

Hydronephrosis in single kidney. (R. Kuss *et al.*) *J. Urol. Néphrol.* 1974, **80**, 471.

Continuous infusion urography in unilateral hydronephrosis. (K. G. Naber *et al.*) *J. Urol.* 1975, **114**, 337.

Caliceal diverticulum. (J. W. Timmons *et al.*) *J. Urol.* 1975, **114**, 6.

Infected pyelocaliceal diverticulum and sympathetic pleural effusion. (M. S. Polsky *et al.*) *J. Urol.* 1975, **114**, 301.

An unusual complication of calyceal diverticulum. (J. L. Nicholas.) *Br. J. Urol.* 1975, **47**, 370.

Our experience of megacalyx (9 cases). (J. C. Masson and A. Shubier.) *J. Urol. Néphrol.* 1975, **81**, 257.

The prognosis of renal obstructions on the basis of radiological data. (R. V. Navarrete. *Minerva Med.* 1975, **66**, 4021.

Physiology and Experimental Observations. Blood-pressure in the rabbit after unilateral inflammatory renal injury. (H. Losse.) *Med. Welt.* 1975, **26**, 1648.

Effect of delayed intermittent catheterisation on kidney function in spinal cord injury patients—a long term follow-up study. (R. Lindan and V. Bellomy.) *Paraplegia*, 1975, **13**, 49.

Renal function in obstructive nephropathy. (A. Ogawa.) *Jpn. J. Urol.* 1975, **66**, 549.

Some specific features of the effect produced by fluothane, chloroform and ether on the renal functions. (B. G. Zhilis *et al.*) *Sov. Med.* 1975, no. 7, July, 104.

Renal function before and after unilateral nephrectomy in renal donors. (R. C. Pabico *et al.*) *Kidney Int.* 1975, **8**, 166.

Polycystic disease and hepatic fibrosis in children—renal function studies. (S. K. Anand *et al.*) *Am. J. Dis. Child.* 1975, **129**, 810.

A scintillation camera technique for quantitative estimation of separate kidney function and its use before nephrectomy. (I. Larsson *et al.*) *Scand. J. Clin. Lab. Invest.* 1975, **35**, 517.

Renal function in obstructive nephropathy—long-term effect of reconstructive surgery. (G. Mayor *et al.*) *Pediatrics*, 1975, **56**, 740.

Age-dependent characteristics of compensatory renal growth. (J. M. Kaufman *et al.*) *Kidney Int.* 1975, **8**, 21.

Position of renal pelvic axis in infant. (P. J. Funke and R. Chiari.) *Urologe*, 1975, **114**, 225.

Distribution of intrarenal blood flow after renal denervation in the dog. (G. Nomura *et al.*) *Nephron*, 1975, **16**, 126.

Renal Failure. Treatment of chronic renal failure by transplantation and dialysis: two decades of cooperation. (N. L. Tilney *et al.*) *Ann. Surg.* 1975, **182**, 108.

Quantitative determination of immunoglobulins in chronic renal failure. (N. Kaliakmanis *et al.*) *Acta Haematol.* (Basel), 1975, **53**, 336.

Acute renal failure following high dose pyelography in patients. (M. Tremblay *et al.*) *Union Med. Can.* 1975, **104**, 1242.

Postoperative renal failure: a new syndrome? (G. E. Merino *et al.*) *Ann. Surg.* 1975, **182**, 37.

Nephrotomography in evaluation of renal failure and masses in infants. (F. G. Baineau *et al.*) *J. Pediatr.* 1975, **87**, 195.

Regular short haemodialysis in end-stage renal failure. (A. M. Martin *et al.*) *Br. Med. J.* 1975, **3**, 758.

Postoperative acute renal failure after operations with extracorporeal circulation. (B. Hasper *et al.*) *Thoraxchirurgie*, 1975, **23**, 392.

Acute renal failure in polytraumatic patients. (J. Lopez *et al.*) *Rev. Clin. Esp.* 1975, **138**, 407.

Anaesthetic considerations in chronic renal failure. (M. Morgan and J. Lumley.) *Anaesth. Intensive Care*, 1975, **3**, 218.

Post-operative renal failure caused by disseminated intravascular coagulation. (A. W. Gotta *et al.*) *Can. Anaesth. Soc. J.* 1975, **22**, 149.

Renal failure and septicemia. (J. Marsac *et al.*) *Rev. Prat.* 1975, **25**, 4193.

Emergency abdominal surgery in cases of chronic renal insufficiency treated by haemodialysis. (L. F. Hollender *et al.*) *Lyon Chir.* 1975, **71**, 318.

Antibiotic therapy and renal insufficiency. (L. Campanacci *et al.*) *Minerva Med.* 1975, **66**, 3547.

Our experience of surgery in patients with uraemia undergoing haemodialysis. (F. Griffanti-Bartoli *et al.*) *Surg. Ital.* 1975, **5**, 125.

Transplantation. Effect of althesin on renal perfusion in anaesthetized dogs. (D. Pataschke *et al.*) *Can. Anaesthst. Soc. J.* 1975, **22**, 138.

Angiographic evaluation of machine perfused kidneys. (K. Dreikorn.) *Urol. Res.* 1975, **3**, 123.

A new organ perfusion system: successful preservation of kidney function for 72 hrs. (R. Grundmann *et al.*) *Langenbecks Arch. Chir.* 1975, **338**, 299.

The renogram and individual ^{131}I-hippuran clearances in experimentally controlled renal perfusion. (B. Hünermann *et al.*) *Urol. Res.* 1975, **3**, 81.

A controlled clinical trial of machine perfusion of cadaveric donor renal allografts. (A. G. R. Sheil *et al.*) *Lancet*, 1975, **2**, 287.

Significance of LDH determination in renal perfusion as criterion of vitality in kidney transplantation. (J. Zinsmeyer *et al.*) *Urol. Int.* 1975, **30**, 362.

A new kidney transport container. A simple vessel for preservation and transport of kidneys and other organs. (W. Hupe.) *Eur. Urol.* 1975, **1**, 193.

Short-term cadaver kidney preservation. (M. Bewick *et al.*) *Br. J. Urol.* 1975, **47**, 501.

Hypothermic storage of the canine kidney for 48 hours in a low chloride solution. (P. R. Schloerb and J. Postel.) *Surg. Gynecol. Obstet.* 1975, **141**, 545.

Preservation of kidneys for transplantation. (M. R. Buhl *et al.*) *Acta Chir. Scand.* 1975, **141**, 310.

Accelerated human renal allograft rejection. (C. B. Anderson and W. T. Newton.) *Arch. Surg.* 1975, **110**, 1230.

Ga-67 citrate in renal allograft rejection. (E. A. George *et al.*) *Radiology*, 1975, **117**, 731.

Influence of ischemia and preservation on condition of arterial system of kidney transplant—microangiographic examinations. 1. Method of examination and normal kidney. 2. [No title given]. (I. S. Amosov and P. M. Kotljatov.) *Radiol. Diagn.* 1974, **15**, 625, 633.

Early detection of acute rejection in renal allografts using radioiodinated autologous fibrinogen. (J. A. Quinlan *et al.*) *Am. J. Surg.* 1975, **130**, 136.

Ex vivo surgery on the renal allograft. (P. J. Van Cangh and G. P. J. Alexandre.) *Eur. Urol.* 1975, **1**, 111.

Ureteroneocystostomy versus ureteropyelostomy: comparison in same renal allograft series. (J. P. Donohue *et al.*) *J. Urol.* 1975, **114**, 202.

Evidence of gentamicin nephrotoxicity in patients with renal allografts. (J. M. Wellwood *et al.*) *Br. Med. J.* 1975, **3**, 278.

Autotransplantation of the kidney for treatment of hydronephrosis due to idiopathic retroperitoneal fibrosis. (A. Puglionisi *et al.*) *Surg. Ital.* 1975, **5**, 135.

Treatment of renal arterial stenosis by autotransplantation in 4 cases. (G. Faure *et al.*) *J. Urol. Néphrol.* 1974, **80**, 514.

Renal autotransplantation. (D. Lange.) *J. Urol. Néphrol.* 1975, **81**, 600.

Bench surgery and renal autotransplantation in the pediatric patient. (J. R. Lilly *et al.*) *J. Pediatr. Surg.* 1975, **10**, 623.

Recurrence of nephrotic syndrome in renal isograft: preliminary report. (J. Matsubara *et al.*) *J. Urol.* 1975, **114**, 779.

Renal transplantation in the rat. I. Studies concerning the ureteral anastomosis with special reference to end-to-end technique. (L. Frödin and A. Engberg.) *Urol. Res.* 1975, **3**, 87.

Renal transplantation in the rat. II. In vitro perfusion of the rat kidneys before transplantation. IV. Cortical pressure gradients measured in vivo and during isolated perfusion with reference to renal function after transplantation. (L. Frödin *et al.*) *Scand. J. Clin. Lab. Invest.* 1975, **35**, 455, 463.

Urological complications in renal transplantation. (K. Dreikorn and L. Rohl.) *Eur. Urol.* 1975, **1**, 170.

Lymphocele formation after renal transplantation. (C. H. Kim and O. C. Fjeldborg.) *Urol. Int.* 1975, **30**, 433

Disseminated aspergillosis in a renal transplant patient—diagnostic difficulties re-emphasised. (H. W. Murray *et al.*) *Johns Hopkins Med. J.* 1975, **137**, 235.

Comprehensive evaluation of renal function in transplanted kidney. (E. V. Dubovsky *et al.*) *J. Nucl. Med.* 1975, **16**, 1115.

Radiological and nuclear diagnosis after kidney-transplantation. (K. J. Pfeifer.) *Fortschr. Med.* 1975, **93**, 1621.

Arterial calcification and progressive peripheral gangrene after renal transplantation. (R. Hällgren *et al.*) *Acta Med. Scand.* 1975, **198**, 331.

Renal transplantation in children. (C. Henriksson *et al.*) *Acta Paediatr. Scand.* 1975, **64**, 833.

Kaposi sarcoma in renal transplant recipient. (C. J. Straehley *et al.*) *Arch. Pathol.* 1975, **99**, 611.

Scintiphotography in evaluation of renal transplants. (H. T. Haden.) *Med. Coll. Va. Q.* 1975, **11**, 101.

Prediction of kidney viability before transplantation. (K. Baxby and R. W. G. Johnson.) *Br. J. Surg.* 1975, **62**, 810.

The effects of iodine contrast media on the function of transplanted kidneys. (J. F. Moreau *et al.*) *Nouv. Presse Méd.* 1975, **4**, 2643.

Immunological follow-up to renal transplant. (H. Friemel.) *Zentralbl. Chir.* 1975, **100**, 1241.

Immunological aid to renal transplant-tissue typing. (G. Funfhausen and K. V. Richter.) *Zentralbl. Chir.* 1975, **100**, 1235.

Late perirenal lymphocele causing ureteral and arterial obstruction in renal transplant patients. (M. G. McLoughlin and G. M. Williams.) *J. Urol.* 1975, **114**, 527.

Avascular necrosis of bone following renal transplantation. (A. M. Pierides *et al.*) *Q. J. Med.* 1975, **44**, 459.

Cine fluoroscopic studies of ureteral function in human renal transplant. (A. Hasegawa *et al.*) *J. Urol.* 1975, **114**, 381.

Hamartoma and renal transplant implications. (S. Feldman *et al.*) *J. Urol.* 1975, **114**, 460.

Hypophyseal-Leydig-cell-function after kidney transplantation. (R. Mies *et al.*) *Med. Welt.* 1975, **26**, 1731.

Prelusive skin grafts in live-donor kidney transplantation. (R. Shackman and J. E. Castro.) *Lancet*, 1975, **2**, 521.

Agonal phase, ischaemic times and renal avascular abnormalities and outcome of cadaver kidney transplants. (C. Hall *et al.*) *Br. Med. J.* 1975, **3**, 667.

Renal homotransplantation in childhood with special reference to the infant recipient and the lymphocyte chalone. (J. R. Lilly *et al.*) *Milit. Med.* 1975, **140**, 626.

Immunoglobulin levels after kidney transplantation and during rejection crisis. (R. Oppolzer *et al.*) *Klin. Wocherschr.* 1975, **53**, 803.

The qualitative nitroblue tetrazolium (NBT) test as a means to differentiate between infection and rejection in renal transplant patients. (R. Sher *et al.*) *Clin. Nephrol.* 1975, **4**, 8.

Blood viscosity factors and occlusive arterial disease in renal transplant recipients. (L. Dintenfass and L. S. Ibels.) *Nephron*, 1975, **15**, 456.

Urologic problems in renal transplantation. (F. J. Leary *et al.*) *Arch. Surg.* 1975, **110**, 1124.

Successful management of caliceal fistulas following renal transplantation. (M. Schiff *et al.*) *Arch. Surg.* 1975, **110**, 1129.

Renal transplantation in the older age group. (F. L. Delmonico *et al.*) *Arch. Surg.* 1975, **110**, 1107.

Fungal infection following renal transplantation. (H. A. Gallis *et al.*) *Arch. Intern. Med.* 1975, **135**, 1163.

Resumption of female reproductive function following renal transplantation. (E. T. Jacob and S. Grünstein.) *Harefuah*, 1975, **89**, 133.

Complicanze mediche dell'omotrapianto renale umano. (F. Quarto di Palo *et al.*) *Minerva Chir.* 1975, **30**, 874.

Criteri immunologici di selezione per il trapianto di rene da cadavere. (G. Sirchia.) *Minerva Chir.* 1975, **30**, 851.

The 12th report of the Renal Transplant Registry. (Advisory Committee to the Renal Transplant Registry, Chicago.) *J.A.M.A.* 1975, **233**, 787.

The organization of organ donation for the transplantation of kidneys. (J. Reichmann and M. Schleusing.) *Dtsch. Gesundh.* 1975, **30**, 1396.

The management of urinary fistulae following cadaveric renal transplantation. (J. G. Brockis *et al.*) *Br. J. Urol.* 1975, **47**, 371.

Ileal conduit in kidney transplantation. (E. T. Jacob *et al.*) *Harefuah*, 1975, **88**, 503.

Leukocyte aggregation test—immunodiagnostic applications and immunotherapeutic implications for clinical renal transplantation. (B. D. Kahan *et al.*) *Arch. Surg.* 1975, **110**, 984.

Occurrence of vesical calculus following renal transplantation. (M. O'Dea *et al.*) *Br. J. Urol.* 1975, **47**, 424.

Arteriography of renal transplants. (W. D. Foley *et al.*) *Radiology*, 1975, **116**, 271.

Conjoined arterial anastomosis: an aid in revascularizing donor kidneys with multiple renal arteries. (L. H. W. Banowsky *et al.*) *Cleve. Clin. Q.* 1975, **42**, 247.

Investigatory Procedures. Selective renal angiography in urotuberculosis. (H. G. Heinz *et al.*) *Forstschr. Med.* 1975, **93**, 1712.

Simultaneous tracing of ^{131}I-Hippuran and ^{197}Hg-chlormerodrin uptake curve in obstructive uropathy. (T. Sakurai *et al.*) *Jpn. J. Urol.* 1975, **66**, 761.

Multi-projectional renal scintigraphy. (R. Seyss.) *Praxis*, 1975, **64**, 1022.

Clinical examinations of the information value of isotope nephrogram after unilateral ureteral occlusion. (R. Voigt.) *Radiobiol. Radiother.* 1975, **16**, 241.

Evaluation of renal and urinary tract abnormalities noted on scintiscans: a retrospective study of 1,711 radioisotope skeletal surveys performed in an 18-month period. (F. T. Maher.) *Mayo Clin. Proc.* 1975, **50**, 370.

Radiology of the urinary tract: some physiological considerations. Annual oration in memory of John S. Bouslog, M.D. 1890-1973. (A. Elkin.) *Radiology*, 1975, **116**, 259.

Edge enhancement of renal X-ray studies. (A. N. Tessler and J. Kossow.) *J. Urol.* 1975, **114**, 435.

Systematic study of the nephrographic times in intravenous urography. 1. Technical problems and normal values. (J. L. Sablayrolles *et al.*) *Ann. Radiol.* 1975, **18**, 543.

New prognostic concepts regarding obstructed kidneys established on the basis of radiological data. (R. V. Navarrete.) *J. Med. Strasbourg*, 1975, **6**, 561.

Urography, shock reaction and repeated urography. (A. F. Lalli.) *Am. J. Roentgen. Radium Ther. Nucl. Med.* 1975, **125**, 264.

Systematic study of the nephrographic times in intravenous urography. 2. Pathological aspects. (F. Joffre *et al.*) *Ann. Radiol.* 1975, **18**, 623.

Persistent nephrogram: sentinel sign of contrast reaction. (J. S. Robbins *et al.*) *J. Urol.* 1975, **114**, 758.

Diagnosis of inflammatory renal diseases with sequence scintigraphy compared to radiological methods. (H. J. Otto *et al.*) *Radiol. Diagn.* 1975, **16**, 505.

Combined use of ultrasound and nuclear medicine techniques in kidney disease. (J. O. Morales and B. B. Goldberg.) *Semin. Nucl. Med.* 1975, **5**, 339.

In vitro studies of subcalyceal upper urinary tract muscle in multicalyceal kidneys. (N. Longrigg.) *Br. J. Urol.* 1975, **47**, 473.

Selective renal venography in the evaluation of a non-functioning hydronephrotic kidney. (O. Adler *et al.*) *Radiol. Clin.* 1975, **44**, 402.

Late haemorrhage following renal biopsy. (R. Gabriel *et al.*) *Br. J. Urol.* 1975, **47**, 358.

Operative Procedures. Supracostal approach to kidney and adrenal. (J. M. Barry and C. V. Hodges.) *J. Urol.* 1975, **114**, 666.

Posterior oblique approach in kidney surgery. (P. Devlesaver.) *J. Urol. Néphrol.* 1974, **80**, 497.

Mechanical device for improved exposure in kidney surgery. (M. E. Jascalevich and H. B. Schwartz.) *J. Urol.* 1975, **114**, 581.

Antireflux procedures in advanced pyelonephritic kidneys—modification of Gregoir operation. (P. Strohmenger and K. Wortberg.) *Urologe*, 1975, **14**, 223.

A technique for chronic repuncture micropuncture of dog kidney. (R. Brewer Auld *et al.*) *Kidney Int.* 1975, **8**, 53.

Permanent nephrostomy via percutaneous puncture. (D. P. Stables *et al.*) *J. Urol.* 1975, **114**, 684.

The avascular nephrotomy. (W. Grégoir.) *Eur. Urol.* 1975, **1**, 57.

URETER

General. Primary amyloidosis of the ureter: case report. (P. G. Klotz.) *Br. J. Urol.* 1975, **47**, 518.

Hernias of the ureter. Anatomic-roentgenographic study. (H. M. Pollack *et al.*) *Radiology*, 1975, **117**, 275.

Retro-caval ureter from a single kidney. (M. Rampal *et al.*) *J. Urol. Néphrol.* 1975, **81**, 627.

Congenital Anomalies. Structure and physiology of congenital megaureters—surgical deductions. (W. Gregoir.) *J. Urol. Néphrol.* 1974, **80**, 457.

Megaureters. (S. N. K. Ghanekar *et al.*) *Clinician*, 1975, **39**, 221.

The ureteric orifice: the embryologic key to radiologic status of duplex kidneys. (G. G. Mackie *et al.*) *J. Pediatr. Surg.* 1975, **10**, 473.

Anastomoses of the urinary tract for treatment of duplicated ureters. (P. Mellin.) *Langenbecks Arch. Chir.* 1975, **340**, 101.

Diagnosis of occult ectopic ureter in duplex kidney. (M. H. Simms and P. M. Higgins.) *J. Urol.* 1975, **114**, 697.

Development of the innervation of the ureter. (C. C. Shulman.) *Eur. Urol.* 1975, **1**, 46.

Double ureter. (H. Melchior.) *J. Urol. Néphrol.* 1974, **80**, 453.

Tumour-like displacement of left ureter caused by an anomaly in position of duodenum. (C. Wernitz and H. Richter.) *Fortschr. Geb. Röntgenstr. Nuklearmed.* 1975, **123**, 186.

Simple ureteral ectopy. (J. R. N. R. Netto *et al.*) *Acta Urol. Belg.* 1975, **43**, 335.

Ureter ectopy in the ejaculatory duct. (A. Demelenne and C. Bouffiuox.) *Acta Urol. Belg.* 1975, **43**, 263.

Crossed-fused renal ectopia with solitary ureter. (N. K. Bissada *et al.*) *J. Urol.* 1975, **114**, 304.

Blind-ending ureter: report of a case and review of the literature. (W. H. Rattner *et al.*) *Bull. Sinai Hosp. Detroit*, 1975, **23**, 159.

Problems and solutions in surgical treatment of 100 consecutive ureteral duplications in children. (D. M. Barrett *et al.*) *J. Urol.* 1975, **114**, 126.

Trauma. Bilateral avulsion of the upper ureters. (A. D. Heath and A. May.) *Br. J. Urol.* 1975, **47**, 386.

Treatment of irradiation injury to the ureter by ileal substitution. (C. P. Perry *et al.*) *Obstet. Gynecol.* 1975, **46**, 517.

Rupture of the ureter below the renal pelvis after closed trauma in a child. (J. Bruezière *et al.*) *J. Urol. Néphrol.* 1975, **81**, 582.

Our therapeutic indications in trauma of the ureter. (R. Banchieri and G. Montalcini.) *U. Urol. Néphrol.* 1975, **81**, 612.

Traumatic rupture of the ureter below the renal pelvis in a child. (M. Revol. *et al.*) *J. Urol. Néphrol.* 1975, **81**, 579.

Early, aggressive management of intraoperative ureteral injuries. (W. H. Hoch *et al.*) *J. Urol.* 1975, **114**, 530.

Fistula. Uretero-vaginal fistulas. (D. V. Kan.) *Sov. Med.* 1975, no. 7, July, 60.

Infections. A case of peri-ureteritis as first sign of carcinoma. (Ch. Richaud *et al.*) *J. Urol. Néphrol.* 1975, **81**, 625.

Xanthogranulomatous ureteritis. (P. Remigio *et al.*) *J. Urol.* 1975, **114**, 621.

Intrinsical ureteral endometriosis. With report of a further case. (S. G. Renders and L. Boccon-Gibod.) *Ann. Urol.* 1975, **9**, 135.

Neoplasms. Bilateral asynchronous primary carcinoma of the ureter. (K. M. Adiga and G. A. Graciansky.) *Int. Surg.* 1975, **60**, 416.

Squamous cell carcinoma of ureterovesical junction after renal transplantation. (R. E. Duncan *et al.*) *J. Urol.* 1975, **114**, 628.

Disseminated metastatic ureteral melanoma. (M. Nakazono *et al.*) *J. Urol.* 1975, **114**, 624.

Primary sarcoma of the ureter. Study of the literature in one personal case. (B. Giraud and M. Rougé.) *J. Urol. Néphrol.* 1975, **81**, 563.

Physiology. Urinary transport in transsected and reanastomosed ureters of dogs. (R. L. Vereecken *et al.*) *Acta Urol. Belg.* 1975, **43**, 282.

The structure and function of the ureter in the dog. (J. Bannigan.) *Ir. J. Med. Sci.* 1975, **144**, 426.

Pathological anatomy of dilated ureter. (G. Debled.) *J. Urol. Néphrol.* 1974, **80**, 521.

Contribution to the study of the development of the terminal portion of the Wolffian duct and the ureter. (A. Tejedo-Mateu *et al.*) *Eur. Urol.* 1975, **1**, 41.

Elastic characteristics of ureter. (D. Walker and B. Finlayson.) *J. Urol.* 1975, **114**, 385.

Ureteral pressure flow studies in difficult diagnostic problems. (V. Marshall and R. H. Whitaker.) *J. Urol.* 1975, **114**, 204.

Studies on action potentials of the upper urinary tract. V. Changes of the ureteral function during and after surgery in patients with calculous disease of the upper urinary tract. (S. Numasato.) *Jpn. J. Urol.* 1975, **66**, 727.

Mechanical Disorders. Vesico-ureteral reflux following transurethral slitting of the ureteral orifice. (P. Nummi and N. Ylönen.) *Ann. Chir. Gynaecol. Fenn.* 1975, **64**, 220.

Some observations and theories on the wide ureter and hydronephrosis. (R. H. Whitaker.) *Br. J. Urol.* 1975, **47**, 377.

Histological findings of the ureteropelvic junction in congenital hydronephrosis. (H. Fladerer and G. Hubmer.) *Urol. Int.* 1975, **30**, 350.

Spontaneous rupture of a ureterocele. (Ch. Viville and J. J. Ludig.) *Ann. Urol.* 1975, **9**, 95.

The simple orthotopic ureterocele in infants. (J. Prévot and M. Schmitt.) *Ann. Urol.* 1975, **9**, 89.

Ureterocele. (M. L. Sussman and A. Newman.) *Ariz. Med.* 1975, **32**, 865.

Ureteroceles in the adult. (G. Soton and R. Gayet.) *Gaz. Med. Fr.* 1975, **82**, 4381.

Multiple ureteral diverticula associated with bilateral ureterocoeles. (I. W. McCall *et al.*) *Br. J. Urol.* 1975, **47**, 538.

Ureteric diverticula. (J. D. Rating.) *Fortschr. Geb. Röntgenstr. Nuklearmed.* 1975, **123**, 184.

Ureteral diverticulum. (D. M. Barrett and R. S. Malek.) *J. Urol.* 1975, **114**, 33.

The pathology of the dilated ureter. (G. Debied.) *Acta Urol. Belg.* 1975, **43**, 301.

Vesicorenal reflux, morphological diagnosis and indications for operation. (R. Stark and P. Bruhl.) *Fortschr. Med.* 1975, **93**, 1243.

Vesico-renal reflux in adults. (P. Hértier and E. Zingg.) *J. Urol. Néphrol.* 1975, **81**, 497.

A review of children operated upon because of stenosis of the pelvo-ureteral junction. (K. Iversen *et al.*) *Int. Urol. Nephrol.* 1975, **7**, 103.

Non-obstructive megacystis and refluxing megaureter in pre-teen enuretic boys with minimal symptoms. (K. J. Welch *et al.*) *J. Urol.* 1975, **114**, 449.

Primary obstructive mega-ureter in adults. (M. Le Guillou *et al.*) *Ann. Urol.* 1975, **9**, 141.

Radiologic diagnosis of mega-ureter in childhood. (K. D. Ebel.) *Roentgenblatter*, 1975, **28**, 297.

Ureteral stenosis after anti-reflux uretero-vesical reimplantation in children. A description of four cases. (C. Viville *et al.*) *Ann. Chir. Infant.* 1975, **16**, 349.

^{99m}Tc-iron complex for demonstrating reflux without use of a catheter. (K. Hahn *et al.*) *Fortschr. Geb. Roentgenstr. Nuklearmed.* 1975, **123**, 321.

Procidentia and ureteric obstruction. (P. R. Riddle *et al.*) *Br. J. Urol.* 1975, **47**, 387.

Ureteral obstruction caused by right ovarian vein. (E. Gunther *et al.*) *Radiologe*, 1975, **15**, 297.

Urinary obstruction in the neonatal infant. (D. J. Alton and P. McDonald.) *Radiol. Clin. N. Am.* 1975, **13**, 343.

Prognostic significance of ureteral obstruction in patients with recurrent carcinoma of cervix uteri. (A. H. Vandyke and J. R. Vannagell.) *Surg. Gynecol. Obstet.* 1975, **141**, 371.

Therapeutic ureteral obstruction and renal artery embolization. (T. J. Thomas *et al.*) *J. Urol.* 1975, **114**, 518.

Vascular distal ureteral obstruction. (B. P. Read and P. C. Devine.) *J. Urol.* 1975, **114**, 762.

Tubular dimensions and juxtaglomerular granulation index in rat kidneys after unilateral obstruction of ureter. A study of the morphogenesis of hydronephrosis. (G. E. Schubert *et al.*) *Urol. Res.* 1975, **3**, 115.

Ureteric obstruction due to uterine prolapse. (R. H. Chapman.) *Br. J. Urol.* 1975, **47**, 531.

Vesicoureteral reflux—reply. (B. R. Girdany.) *J. Pediatr.* 1975, **87**, 1012.

Vesicoureteral reflux. (P. R. Lewy and A. B. Belman.) *J. Pediatr.* 1975, **87**, 1012.

Vesicoureteral reflux in babies with myelomeningocele. (R. V. Magnus.) *J. Urol.* 1975, **114**, 122.

Investigatory Procedures. Routine isotopes cystography using ^{99M}TC sulfur colloid for detection and follow-up of vesicoureteral reflux. (I. Nissenkorn *et al.*) *Harefuah*, 1975, **89**, 349.

The effect of acute chemical sympathectomy on the competence of the canine ureterovesical junction. (A. J. Wein *et al.*) *Urol. Res.* 1975, **3**, 95.

Investigation of ureteric function with simultaneous intraureteric pressure recordings and ureteropyelography. (U. Ulmsten and J. Diehl.) *Radiology*, 1975, **117**, 283.

Merlin modification of ureteral catheters. (H. E. Merlin *et al.*) *J. Urol.* 1975, **114**, 109.

Operative Procedures. Antireflex ureterocystostomy at the vertex of the bladder. (I. Bradić *et al.*) *Br. J. Urol.* 1975, **47**, 525.

Uretero-colic anastomosis by the "cuff" or "flap" procedure—Goodwin's modified technique. Preliminary report. (A. Steg and L. Boccon Gibod.) *Eur. Urol.* 1975, **1**, 159.

The prosthetic replacement of the ureter. Experimental and clinical results. (B. Dufour and P. Blondel.) *Eur. Urol.* 1975, **1**, 134.

Ureteral replacement: indications, technique and results. (R. S. Ferracani.) *Prensa Méd. Argent.* 1975, **62**, 287.

Suspended segmental ureter replacement—current situation. (B. Dufour *et al.*) *J. Urol. Néphrol.* 1974, **80**, 437.

Silicone ureter prosthesis—preliminary results with dogs. (F. Hennebert.) *J. Urol. Néphrol.* 1974, **80**, 429.

Considerations on ureter replacement by prosthesis of silicone elastomer—3 cases . (J. Leemans and A. Kotowicz.) *J. Urol. Néphrol.* 1974, **80**, 424.

Auto transplantation of the ureter in its whole length in animal experiments. (W. Esch.) *Acta Chir. Aust.* 1975, **7**, 101.

Comments on problems of uretero-ileo-cystoplasty (P. Lichtenauer *et al.*) *Urologe*, 1975, **14**, 217.

Retrograde ureterocystography by suprapubic puncture. Technique and complications. (Ch. Viville *et al.*) *Ann. Urol.* 1975, **9**, 167.

The operative repair of megaureter in children. (P. Hennebert *et al.*) *Acta Urol. Belg.* 1975, **43**, 313.

Ureteropyelostomy with flaps with an everted suture. (G. Mobilio and S. C. Cunico.) *Urol. Int.* 1975, **30**, 397.

Uretero-calicostomy. (S. Wesolowski.) *Eur. Urol.* 1975, **1**, 18.

Irregular regeneration and diverticulum formation after intubated ureterotomy. (A. Borkowski.) *Eur. Urol.* 1975, **1**, 91.

Transvesical ureterotomy. (J. M. Gil-Vernet *et al.*) *Cir. Esp.* 1975, **29**, 79.

Indications for cutaneous ureterostomy—experience with 117 cases. (W. Wagner.) *Urologe*, 1975, **14**, 213.

Catheterless cutaneous ureterostomy. (A. Ariyoshi *et al.*) *J. Urol.* 1975, **114**, 533.

Cutaneous transureterostomy in children. (G. Béland and I. Laberge.) *J. Urol.* 1975, **114**, 588.

Sigmoidoproctoureterostomy—technique for withdrawing urine. (A. Tramoyerescelma *et al.*) *J. Urol. Néphrol.* 1974, **80**, 540.

Indications for ureterostomy. (J. Brueziere.) *J. Urol. Néphrol.* 1974, **80**, 319.

Ureteroneocystostomy by means of modified triangular flap method. (H. Taguchi *et al.*) *J. Urol.* 1975, **114**, 705.

Trans-uretero-ureterostomy: British experience. (I. B. Smith and J. C. Smith.) *Br. J. Urol.* 1975, **47**, 519.

URACHUS

Mucouria in urachal adenoma. (K. Maar *et al.*) *Urologe*, 1975, **114**, 240.

BLADDER

General. Primary amyloidosis of bladder. (K. K. Au and J. H. Gilbaugh.) *J. Urol.* 1975, **114**, 786.

Post-obstructive diuresis. (N. Baum *et al.*) *J. Urol.* 1975, **114**, 53.

Simple method of residual urine determination without bladder catheterization. (R. Hintze *et al.*) *Dtsch. Med. Wochenschr.* 1975, **100**, 2565.

Experiences with suprapubic bladder drainage following gynecological surgery. (G. Raber *et al.*) *Zentralbl. Gynaekol.* 1975, **97**, 1263.

Evolution of bladder statics in spina bifida. (M. Leguillou *et al.*) *J. Urol. Néphrol.* 1974, **80**, 326.

Bladder dysfunction after Schauta hysterectomy. One-year follow-up. (D L. Barclay and J. J. Romanlopez.) *Am. J. Obstet. Gynecol.* 1975, **123**, 519.

Effect of therapy on bladder motility in patients with radiologically treated cervical carcinoma. (M. Kaczmarek *et al.*) *Zentralbl. Gynaekol.* 1975, **97**, 1260.

Woodworm and the bladder. (C. G. C. Gaches.) *Proc. R. Soc. Med.* 1975, **68**, 525.

Congenital Anomalies. Exstrophy of bladder. 1. Long-term results in series of 37 cases treated by ureterosigmoidostomy. (H. M. Spence *et al.*) *J. Urol.* 1975, **114**, 133.

Surgical treatment of bladder exstrophy. (J. de Leval and Ch. Bouffioux.) *Acta Urol. Belg.* 1975, **43**, 292.

Accessory exstrophic bladder. (M. H. Saadi.) *Br. J. Clin. Pract.* 1975, **29**, 275.

Long-term results of ureterosigmoidostomy in children with bladder exstrophy. (J. W. Segura and P. P. Kelalis.) *J. Urol.* 1975, **114**, 138.

One-stage reconstruction for exstrophy of the bladder in girls. (Discussion by C. J. Devine.) *Plast. Reconstr. Surg.* 1975, **56**, 209.

Trauma. Bladder of patients with medullary trauma. (M. Maury.) *J. Urol. Néphrol.* 1974, **80**, 241.

Non-operative treatment of ruptured bladder. (J. R. Richardson and G. W. Leadbetter.) *J. Urol.* 1975, **114**, 213.

Fistula. Bladder fistula following total hip replacement using self-curing acrylic. (J. D. Lowell *et al.*) *Clin. Orthop.* 1975, no. 111, Sept. 131.

Infections. Auto-immune interstitial cystitis. (D. Lange.) *J. Urol. Néphrol.* 1975, **81**, 603.

Epidemiology of interstitial cystitis. (K. J. Oravisto.) *Ann. Chir. Gynaecol. Fenn.* 1975, **64**, 75.

Cystitis glandularis causing bilateral ureteric obstruction and hydronephrosis. (K. G. Rao.) *Br. J. Urol.* 1975, **47**, 398.

Intravesical formalin for control of intractable bladder hemorrhage secondary to cystitis or cancer. (S. Kumar *et al.*) *J. Urol.* 1975, **114**, 540.

Routing current cystitis. *Emergen. Med.* 1975, 7, 118.

A new drug for the treatment of radiation cystitis. (H. Marberger *et al.*) *Curr. Ther. Res.* 1975, **18**, 466.

Angiography in urinary bladder tuberculosis. (S. O. Hietala and M. Duchek.) *Acta Radiol.* 1975, **16**, 297.

Calculi. Blind litholapaxy—medico-historical curiosity or a well-established procedure. (W. Mauermayer.) *Aktuel. Urol.* 1975, **6**, 257.

Urinary bladder stones as a complication after gynecologic-surgical treatment. (M. S. Litschgi *et al.*) *Fortschr. Med.* 1975, **83**, 1627.

Ultrasonic lithotrity for stones of bladder. (Lutzeyer.) *J. Urol. Néphrol.* 1974, **80**, 464.

Neoplasms. Diagnosis and treatment of sarcoma botryoides. (H. Frohmüller and R. Ackermann.) *Urol. Int.* 1975, **30**, 420.

Desmoid tumor involving bladder. (J. W. Foote *et al.*) *J. Urol.* 1975, **114**, 147.

The effect of sex hormones on the incidence of experimental urinary bladder tumors in rats. (N. Kono *et al.*) *Jpn. J. Urol.* 1975, **66**, 409.

Value of mechanical cell harvesting in diagnosis and prognosis of bladder tumor recurrence. (A. Morales *et al.*) *J. Urol.* 1975, **114**, 220.

Mitomycin C bladder instillation therapy for bladder tumors. (T. Mishina *et al.*) *J. Urol.* 1975, **114**, 217.

Haematuria following radiotherapy for bladder tumours. An approach to therapy. (G. Dell'Adami and A. Brunetti.) *Urol. Int.* 1975, **30**, 326.

Inverted papillomas of urinary bladder. (I. J. Demeester *et al.*) *Cancer*, 1975, **36**, 505.

An epidemiological study of occupational bladder tumours in the dye industry of Japan. (K. Tsuchiya *et al.*) *Br. J. Industr. Med.* 1975, **32**, 203.

Pseudo-tumors of the urinary bladder. (M. Bonard *et al.*) *Ann. Urol.* 1975, **9**, 69.

Hyperthermic treatment for the bladder tumor. 1. Clinical study. (T. Kishimoto *et al.*) *Jpn. J. Urol.* 1975, **66**, 485.

Effects of sex hormones on development of urinary bladder tumours in rats induced by N-Butyl-N-(4-Hydroxybutyl) Nitrosamine. (E. Okajima *et al.*) *Urol. Res.* 1975, **3**, 73.

On the local treatment of urinary bladder tumours with peptichemio. (T. Battelli *et al.*) *Panminerva Med.* 1975, **17**, 262.

TNM classification of malignant tumours of the bladder, prostate, testis and kidney. (W. E. Collins.) *Can. J. Surg.* 1975, **18**, 468.

Papillary urothelial tumor of the bladder in a child. (G. Waaler *et al.*) *J. Pediatr. Surg.* 1975, **10**, 841.

Therapeutic problems posed by association of bladder tumor and prostatic adenoma. (M. Leguillou *et al.*) *J. Urol. Néphrol.* 1974, **80**, 554.

Bladder tumors in children. (E. Perezcastro.) *J. Urol. Néphrol.* 1974, **80**, 551.

Evaluation of lymphangiography for clinical staging of bladder tumors. (Z. Wajsman *et al.*) *J. Urol.* 1975, **114**, 712.

Experiences based on the classification of bladder tumours according to the TNM system. (H. Vogler *et al.*) *Eur. Urol.* 1975, **1**, 93.

Diagnostic and therapeutic patterns of bladder tumours. (N. Mallo and J. Vicente.) *Eur. Urol.* 1975, **1**, 96.

Classification of bladder tumours. (D. M. Wallace.) *Eur. Urol.* 1975, **1**, 65.

Fibrinolytic enzyme system in blood of rats with urinary bladder tumor induced by oral administration of N-Butyl-N-(4-hydroxybutyl) nitrosamine. (N. Kono *et al.*) *Jpn. J. Urol.* 1975, **66**, 742.

New method for determination of urinary tryptophan metabolites in bladder carcinoma. (N. A. Romas *et al.*) *J. Urol.* 1975, **114**, 223.

Carcinoma of the bladder complicating cyclophosphamide therapy. (I. D. Ansell and J. E. Castro.) *Br. J. Urol.* 1975, **47**, 413.

Squamous carcinoma in a squamous-lined bladder. (I. G. Kidson *et al.*) *Proc. R. Soc. Med.* 1975, **68**, 522.

Haematoporphyrins in the diagnosis and treatment of carcinoma of the bladder. (J. F. Kelly.) *Proc. R. Soc. Med.* 1975, **68**, 527.

Carcinoma of the urinary bladder in patients receiving cyclophosphamide. (R. L. Wall and K. P. Clausen.) *N. Engl. J. Med.* 1975, **293**, 271.

Post-diversion pre-cystectomy irradiation for carcinoma of the bladder. (E. M. Mahoney *et al.*) *J. Urol.* 1975, **114**, 46.

Squamous carcinoma of bladder with pseudosarcomatous stroma. (W. Jao *et al.*) *Arch. Pathol.* 1975, **99**, 461.

Arterial infusion of 5-FU as a therapeutic adjunct in the treatment of advanced carcinoma of bladder and prostate. (J. E. Nevin *et al.*) *Va. Med. Mon.* 1975, **102**, 614.

Immunological detection of human bladder carcinoma. (A. P. Monaco *et al.*) *Ann. Surg.* 1975, **182**, 325.

Further observations on carcinoma in situ of urinary bladder—silent but extensive intraprostatic involvement. (T. A. Seemayer *et al.*) *Cancer*, 1975, **36**, 514.

Prophylactic use of thio-tepa and urokinase in transitional cell carcinoma of bladder: preliminary report. (H. Hisazumi *et al.*) *J. Urol.* 1975, **114**, 394.

Carcinoma of bladder T3NXMO treated by preoperative irradiation followed by cystectomy—3rd Report of Rotterdam Radio-Therapy Institute. (B. H. P. Vanderwerfmessing.) *Cancer*, 1975, **36**, 718.

A low dose-fractionation scheme for the radiotherapy of carcinoma of the bladder. Experimental background and preliminary results. (B. Littbrand *et al.*) *Bull. Cancer*, 1975, **61**, 241.

Clinical and experimental studies on carcinoma of the bladder. (T. Niijima.) *Jpn. J. Urol.* 1975, **66**, 527.

The cytology of transitional cell carcinoma of the urinary bladder. (W. H. Kern.) *Acta Cytol.* 1975, **19**, 420.

Urine cytology and bladder carcinoma. (D.Völter and H. Ziegler). *Dtsch. Med. Wochenschr.* 1975, **100**, 2340.

Measurement of urinary cea-like substance—aid in management of patients with bladder carcinoma. (B. Wahren *et al.*) *Cancer*, 1975, **36**, 1490.

Bladder carcinoma involving lower abdominal wall. (R. B. Bracken and H. Grabstadt.) *J. Urol.* 1975, **114**, 715.

The treatment of bladder carcinoma. (J. A. Martinez-Piñeiro.) *Eur. Urol.* 1975, **1**, 68.

Metastases to eye from transitional cell carcinoma of bladder. (M. I. Resnick *et al.*) *J. Urol.* 1975, **114**, 722.

New aspects in combined treatment of urinary bladder carcinoma. (L. Albert *et al.*) *Eur. Urol.* 1975, **1**, 117.

Carcinoma of the bladder: present state of therapy. (E. Zingg.) *Praxis*, 1975, **64**, 1550.

Alterations of serum lactic dehydrogenase and its isoenzyme V fraction levels following hyperglycemic condition in patients with bladder carcinoma. (T. Ishibe *et al.*) *Urol. Int.* 1975, **30**, 437.

Ring calcification in a bladder phaeochromocytoma. (T. M. Kolawale *et al.*) *Br. J. Radiol.* 1975, **48**, 931.

Pheochromocytoma of bladder—new case. (A. Benchekroun *et al.*) *J. Urol. Néphrol.* 1974, **80**, 546.

Clinical evaluation of urinary and serum carcinoembryonic antigen in bladder cancer. (R. A. Fraser *et al.*) *J. Urol.* 1975, **114**, 226.

Saccharin and bladder cancer. *Br. Med. J.* 1975, **3**, 610.

Single and combination chemotherapy for primary murine bladder cancer. (M. S. Soloway) *Cancer*, 1975, **36**, 333.

Partial cystectomy in treatment of bladder cancer. (R. A. Evans and J. H. Texter.) *J. Urol.* 1975, **114**, 391.

Chemoprophylaxis of bladder cancer recurrence: immunological aspects. (F. Corrado *et al.*) *Panminerva Med.* 1975, **17**, 253.

Bladder cancer—results of radiation therapy in 384 patients. (D. R. Goffinet *et al.*) *Radiology*, 1975, **117**, 149.

Transplantable strains of urinary bladder cancer and hemangiopericytoma, obtained by transplantation of fetal urinary bladder tissue. (T. V. Osipova *et al.*) *Vopr. Oncol.* 1975, **21**, 89.

Conservative management of distal large bowel cancer invading the urinary bladder. (H. W. Whiteley and H. Grabstald.) *Clin. Bull.* 1975, **5**, 99.

Studies on plasminogen activator activity in cancerous tissues of the bladder. (A. Kojima.) *Jpn. J. Urol.* 1975, **66**, 753.

Malignant phaeochromocytoma of the urinary bladder—report of two cases. (P. Javaheri and J. Raafat.) *Br. J. Urol.* 1975, **47**, 401.

Rabdomiosarkoon van die Blass (rhabdomyosarcoma of the bladder). (P. J. Malan.) *S. Afr. Med. J.* 1975, **49**, 1404.

The late results of ileal conduit diversion with special reference to the survival rates on bladder malignancies. (H. Tazaki.) *Jpn. J. Urol.* 1975, **66**, 493.

Malignant metastatic melanoma of the bladder. (D. A. Tolley *et al.*) *Br. J. Clin. Pract.* 1975, **29**, 276.

Experimental Investigations. Use of failbaryt as contrast medium for cystography. (U. Retzke and H. Retzke.) *Zentralbl. Gynaekol.* 1975, **97**, 1239.

The excretion-miction-cystourethrography (EMCU) following an intensive urography. (G. Otto-Unger.) *Dtsch. Gesundh.* 1975, **30**, 1849.

Interrelationship between plasminogen activator activity and tissue repair of the bladder. (H. Sugiura and T. Astrup.) *Jpn. J. Urol.* 1975, **66**, 689.

Replacement of urinary bladder wall in the cat by autologous X-ray treated full thickness skin graft. (R. Pust *et al.*) *Urol. Res.* 1975, **3**, 139.

The effect of chlorhexidine irrigation of the bladder in the rat. (W. E. S. Harper and L. R. Matz.) *Br. J. Urol.* 1975, **47**, 539.

Hydrostatic bladder distension—physiology and clinical application. (J. C. Smith *et al.*) *Eur. Urol.* 1975, **1**, 75.

Myotropic electrostimulation of bladder—experimental research. (H. Melchior *et al.*) *J. Urol. Néphrol.* 1974, **80**, 443.

Urinary bladder effects of levodopa in hamsters. (W. A. Croft.) *Arch. Pathol.* 1975, **99**, 473.

Vascular and morphological changes in the urinary bladder wall after irradiation. (S. O. Hietala *et al.*) *Int. Urol. Néphrol.* 1975, **7**, 119.

Mechanical Disorders *see* **Micturition.**

Operative Procedures. Modification of evacuator. (C. W. Hayes and D. D. Schlapik.) *J. Urol.* 1975, **114**, 110.

Neo-bladder made from the rectum in surgical cure of uro-genital malformations. (M. Nédelec *et al.*) *J. Urol. Néphrol.* 1975, **81**, 481.

An improved surgical technique for intravesical resection of bladder diverticula. (A. H. Colodny.) *Br. J. Urol.* 1975, **47**, 399.

Duraplasty of the urinary bladder—results after two to six years. (A. Kelami.) *Eur. Urol.* 1975, **1**, 178.

Experience with extended use of Foley catheter following repair of bladder. (M. Rosenberg.) *Surg. Gynecol. Obstet.* 1975, **141**, 734.

PROSTATE

General. Diseases of the prostate: an outline to diagnosis and treatment. (N. K. Bissada and J. F. Redman.) *J. Arkansas Med. Soc.* 1975, **72**, 235.

Infections and Prostatitis. The perplexing problem of prostatitis. (N. R. Zinner.) *Postgrad. Med.* 1975, **58**, 96.

The status of the sexual function in patients with chronic prostatitis. (M. I. Kaplun.) *Vestn. Dermatol. Venerol.* 1975, no. 6, June, 65.

Semen cultures in diagnosis of bacterial prostatitis. (D. F. Mobley.) *J. Urol.* 1975, **114**, 83.

The bacteriology of prostatitis and infertility. (A. H. Horan.) *Conn. Med.* 1975, **39**, 407.

Benign Prostatic Hypertrophy. Altered blood androgens in elderly men with prostate hyperplasia. (R. Horton *et al.*) *J. Clin. Endocrinol. Metab.* 1975, **41**, 793.

Prostatic hypertrophy. (S. Davilaaguinaga.) *Rev. Bras. Med.* 1975, **32**, 580.

Androgen-binding proteins in human benign prostatic hypertrophy. (V. Rosen *et al.*) *J. Clin. Endocrinol. Metab.* 1975, **41**, 761.

Treatment of benign prostatic hypertrophy with flutamide (SCH 13521); placebo-controlled study. (M. Caine *et al.*) *J. Urol.* 1975, **114**, 564.

Indications and results of cryosurgery in 47 high risk patients with prostatic hypertrophy or carcinoma. (G. Anselmo *et al.*) *Endoscopy*, 1975, **7**, 146.

Carcinoma. External-beam megavoltage radiation therapy in treatment of post-radical prostatectomy, residual or recurrent tumor: preliminary results. (G. R. Ray *et al.*) *J. Urol.* 1975, **114**, 98.

Leiomyosarcoma of the prostate. (A. C. Chatterjee.) *Br. J. Urol.* 1975, **47**, 577.

Malignant prostatic cystosarcoma phyllodes. (B. Gueft and M. A. Walsh.) *N.Y. State J. Med.* 1975, **75**, 2226.

Cure of an adult prostatic sarcoma. (P. Leger.) *J. Urol. Néphrol.* 1975, **81**, 527.

Treatment of prostatic cancer with estracyt^R (estramustine phosphate). (F. Balogh and Kisbenedek.) *Int. Urol. Néphrol.* 1975, **7**, 135.

The epidemiology of cancer of the prostate. (I. T. T. Higgins.) *J. Chronic Dis.* 1975, **28**, 343.

Prevention of body fluid retention by furosemide during estrogen therapy of prostatic cancer. (M. J. Kontturi and E. A. Sotaniemi.) *J. Urol.* 1975, **114**, 251.

Isochromosome 17 in prostatic cancer. (M. Oshimura and A. A. Sandberg.) *J. Urol.* 1975, **114**, 249.

Radiation therapy of cancer of the prostate. (J. F. Wilson and J. D. Cox.) *Wis. Med. J.* 1975, **74**, S/98.

Tumoricidal steroids: potential cure for advanced breast and prostatic cancer. (R. E. Buller.) *Tex. Med.* 1975, **71**, 86.

Our present therapeutic procedure in prostatic cancer. (U. Bracci and F. di Silverio.) *G. Gerontol.* 1975, **23**, 287.

Action of estrogens in treatment of prostatic cancer—pyknotic index and cytology of prostate cells. (K. H. Kurth *et al.*) *J. Urol. Néphrol.* 1974, **80**, 453.

The choice of estrogen preparations in the treatment of prostatic cancer. (A. Morales and B. Pujari.) *Can. Med. Assoc. J.* 1975, **113**, 865.

The effectiveness of transrectal aspiration cytology in the diagnosis of prostatic cancer. (R. Sonnenschein.) *Eur. Urol.* 1975, **1**, 189.

Orbital metastasis from prostatic carcinoma. (T. Usui *et al.*) *Br. J. Urol.* 1975, **47**, 458.

Inhibition of platelet aggregation caused by estrogen treatment in patients with carcinoma of prostate. (M. Eisen *et al.*) *J. Urol.* 1975, **114**, 93.

Urinary polyamine levels in diagnosis of carcinoma of prostate. (W. R. Fair *et al.*) *J. Urol.* 1975, **114**, 88.

High voltage irradiation for prostatic carcinoma. (R. Denis.) *Ann. Urol.* 1975, **9**, 73.

Radiation enteritis following radiotherapy for prostatic carcinoma. (F. J. Duggan *et al.*) *Br. J. Urol.* 1975, **47**, 441.

Carcinoma of prostate: study of 213 patients with stage C tumors treated by total perineal prostatectomy. (F. H. Schroeder and E. Belt.) *J. Urol.* 1975, **114**, 257.

Suppression of plasma androgens by spironolactone in castrated men with carcinoma of prostate. (P. C. Walsh and P. K. Siiteri.) *J. Urol.* 1975, **114**, 254.

Hydroxyurea in stage D carcinoma of prostate: pilot study. (H. Lerner *et al.*) *J. Urol.* 1975, **114**, 425.

Bone marrow acid phosphatase in staging prostatic carcinoma. (J. E. Pontes *et al.*) *J. Urol.* 1975, **114**, 422.

Surgery of prostatic carcinoma. (R. H. Flocks *et al.*) *Cancer*, 1975, **36**, 705.

External beam radiation therapy of primary carcinoma of prostate. (M. A. Bagshaw *et al.*) *Cancer*, 1975, **36**, 723.

Prostatic carcinoma: treated at categorical center, 1960-1969. (G. P. Murphy *et al.*) *N.Y. State J. Med.* 1975, **75**, 1663.

Palliative treatment with oral estracyt in disseminated prostatic carcinoma. (K. Welvaart.) *Arch. Chir. Neerl.* 1975, **27**, 193.

Histological study on prostatic carcinoma—prognostic and therapeutic importance. (C. Bouffioux.) *J. Urol. Néphrol.* 1974, **80**, 531.

Radiologic detection of prostatic carcinoma by double contrast retrograde urethrocystography. (W. Wong *et al.*) *J. Urol.* 1975, **114**, 746.

Use of arterial infusion of 5-fluorouracil either alone or in combination with supervoltage radiation as a treatment for carcinoma of prostate and bladder. (J. E. Nevin.) *Am. J. Surg.* 1975, **130**, 544.

Proof of metastases by lymphography on prostatic carcinoma. (A. Rost *et al.*) *Urol. Int.* 1975, **30**, 402.

The actual state of diagnostics and therapy of carcinoma of the prostate. (R. Nagel.) *Praxis*, 1975, **64**, 1529.

Delayed cutaneous hypersensitivity in patients with prostatic adenocarcinoma. (J. C. Huus *et al.*) *J. Urol.* 1975, **114**, 86.

Obstruction. The female prostate updated. (T. Moore.) *Eur. Urol.* 1975, **1**, 32.

Physiology and Experimental Study. Ultrastructure of anterior lobe epithelium of the prostate of rat. 1. Initial changes in epithelial cells following administration of estrogen. (K. Yoshida.) *Jpn. J. Urol.* 1975, **66**, 383.

Androgen binding proteins in hyperplastic human prostate—methodological aspects. (J. Y. Dubé *et al.*) *Union Med. Can.* 1975, **104**, 1224.

Stromal hypocellularity and encapsulation in organ cultures of human prostate. Application in epithelial cell isolation. (M. M. Webber and O. G. Stonington.) *J. Urol.* 1975, **114**, 246.

Role of lactogen in prostatic physiology. (W. E. Farnsworth.) *Urol. Res.* 1975, **3**, 129.

Doxycycline levels in prostatic tissue and blood. (W. Mathisen *et al.*) *Eur. Urol.* 1975, **1**, 157.

Evidence for a specific dihydrotestosterone-binding cytosol receptor in the human prostate. (J. Geller *et al.*) *J. Clin. Endocrinol. Metab.* 1975, **41**, 854.

Operative Procedures. Millins operation under reduced pressure. (M. R. Welsch.) *J. Urol. Néphrol.* 1974, **80**, 505.

Two new types of cystoscopic forceps for versatile fluorescence cystoscope. (I. Nakano *et al.*) *J. Urol.* 1974, **114**, 761.

Bladder explosions during transurethral surgery. (T. C. Ning *et al.*) *J. Urol.* 1975, **114**, 536.

Eye injury during transurethral surgery. (S. D. Thomas.) *J. Urol.* 1975, **114**, 584.

Transurethral electroresection with continuous waterflow through a new resectoscope. (H. Geister *et al.*) *Urologe*, 1975, **114**, 232.

Changes in the male urethra produced by instrumentation for transurethral resection of the prostate. (W. A. Shaver *et al.*) *Radiology*, 1975, **116**, 623.

Results of internal urethrotomy of bulbous urethral stenosis in chronic prostatitis. (R. Chiari *et al.*) *Aktuel. Urol.* 1975, **6**, 165.

Prostate and transurethral resection in poor surgical risk patients. A comparative clinical follow-up study. (K. Möhring *et al.*) *Urol. Int.* 1975, **30**, 414.

Prostatic cryoresection (association of cryosurgery and transurethral resection)—technical indications and results. (G. Rigondet *et al.*) *J. Urol. Néphrol.* 1974, **80**, 506.

Prostatectomy in patients with blood disorders and diseases. (E. Merimsky *et al.*) *J. Urol. Néphrol.* 1974, **80**, 502.

Transurethral resection of prostate. (Orandi.) *J. Urol. Néphrol.* 1974, **80**, 462.

Effective drainage of the bladder after transvesical prostatectomy. (P. Nummi and J. Tiitinen.) *Ann. Chir. Gynaecol. Fenn.* 1975, **64**, 217.

Retropubic prostatectomy. Personal technique avoiding hemorrhage in 3,000 cases. (F. Gallizia *et al.*) *J. Urol. Néphrol.* 1975, **81**, 608.

Nitroprusside for control of post-prostatectomy bleeding. (S. C. Evins *et al.*) *J. Urol.* 1975, **114**, 645.

Presentation of distal borderline in TUR resection of prostate. (K. Fleischmann.) *Urologe*, 1975, **14**, 245.

Modification of Young procedure for radical perineal prostatectomy. (J. S. Wheeler.) *J. Urol.* 1975, **114**, 419.

Transurethral prostatectomy in patients with severe hip deformity. (N. K. Bissada *et al.*) *J. Urol.* 1975, **114**, 417.

Experience and results with cryosurgery of prostate. (G. Staehler *et al.*) *Aktuel. Chir.* 1975, **10**, 263.

URETHRA

Congenital Anomalies. Congenital polyp of prostatic urethra in child. (E. J. Braun.) *J. Urol.* 1975, **114**, 311.

The incidence of hypospadias in Sweden. (L. Avellán.) *Scand. J. Plast. Reconstr. Surg.* 1975, **9**, 129.

A long-term follow-up of hypospadias patients. (B. C. Sommerlad.) *Br. J. Plast. Surg.* 1975, **28**, 324.

Surgery of hypospadias. (A. Buschmann.) *Langenbecks Arch. Chir.* 1975, **339**, 421.

Distal hypospadias, chordee and torsion: Allen-Spence procedure and new modifications. (G. T. Klauber.) *J. Urol.* 1975, **114**, 765.

Hypospadias: a general review. (J. E. Keeton and T. C. Fenter.) *J. Miss. State Med. Assoc.* 1975, **16**, 340.

Hypospadias—follow-up study after prenuptial Y-V-plasty. (K. O. Viddal and R. Bjordal.) *Z. Kinder. Chir. Grenzgeb.* 1975, **17**, 243.

Hypospadias in infancy. 1. Pathophysiologic considerations. 2. Hormonal balance studies. (J. Glatzl.) *Paediatr. Paedol.* 1975, **10**, 420.

Mathematical planning for local plasty in hypospadias. (D. D. Murvanidze and S. Y. Kocharova.) *Acta Chir. Plast.* 1975, **17**, 20.

At what age should hypospadias be operated? (M. Boureau.) *Rev. Prat.* 1975, **25**, 3145.

Hypospadias repair using polyglycolic acid sutures. (M. Gipson.) *Br. J. Plast. Surg.* 1975, **28**, 135.

Epispadias without bladder exstrophy in a female. (W. Bischoff and F. Schindera.) *Urologe*, 1975, **14**, 235.

An assessment of the functional results of various forms of surgery for epispadias and exstrophy. (H. B. Eckstein.) *Langenbecks Arch. Chir.* 1975, **339**, 439.

Duplication of the urethra. (H. Muller.) *Z. Kinder. Chir. Grenzgeb.* 1975, **17**, 278.

Trauma. Rupture of the female urethra in childhood. (D. I. Williams.) *Eur. Urol.* 1975, **1**, 129.

Traumatic ruptures of the urethra in children. (J. Aubert and B. Court.) *Eur. Urol.* 1975, **1**, 122.

Posttraumatic constriction of bulbar urethra. (E. N. Netto.) *J. Urol. Néphrol.* 1974, **80**, 552.

Traumatic lesions of the urethra—immediate and delayed treatment. Round table discussion. *Eur. Urol.* 1975, **1**, 3.

Management of non-penetrating distal urethral trauma. (H. L. Kiracofe *et al.*) *J. Urol.* 1975, **114**, 57.

Radiation injuries of urethra and bladder. (P. Lichtenauer and H. Reme.) *Zentralbl. Chir.* 1975, **100**, 833.

First aid and general principles of treatment of urethral injuries accompanying pelvic fractures. (J. Zielinski.) *Int. Urol. Nephrol.* 1975, **7**, 131.

Fistula. Silicone and rubber casts of the distal urethra in studying fistula formation and other hypospadias problems. (P. L. G. Townsend.) *Br. J. Plast. Surg.* 1975, **28**, 320.

Operative correction of recurrent recto-vaginal and urethro-vaginal fistulas. (A. M. Holschneider and W. C. Hecker.) *Z. Kinder. Chir. Grenzgeb.* 1975, **17**, 227.

Infections and Urethral Syndrome. Intensive and prolonged tetracycline therapy in non-specific urethritis. (N. Helmy and W. Fowler.) *Br. J. Vener. Dis.* 1975, **51**, 336.

Evaluation of a sustained-release oral tetracycline in non-specific urethritis. (P. M. Perera.) *Br. J. Vener. Dis.* 1975, **51**, 333.

The treatment of non-specific urethritis. (G. Heap.) *Med. J. Aust.* 1975, **2**, 831.

Stricture. Symphysiotomy for transpubic approach to traumatic strictures of the posterior urethra. (C. Chatelain *et al.*) *Eur. Urol.* 1975, **1**, 140.

Bladder neck contracture and urethral stricture as complications of renal transplantation. (S. A. Loening *et al.*) *J. Urol.* 1975, **114**, 688.

Use of the Otis urethrotome in the treatment of urethral strictures and congenital urethral stenoses. (H. Frohmüller and H. Bülow.) *Eur. Urol.* 1975, **1**, 87.

New technique to aid catheterization of traumatized urethral stricture. (N. M. Heney.) *J. Urol.* 1975, **114**, 725.

Transpubic approach for strictures of membranous urethra. (T. D. Allen.) *J. Urol.* 1975, **114**, 63.

Pediatric urology—are you missing significant urethral stenosis. (R. L. Helmling *et al.*) *Patient Care*, 1975, **9**, 120.

Calculi. Considerations on urethral stones. (J. Neveu.) *Sem. Hop. Paris*, 1975, **51**, 425.

Neoplasms. Primary adenocarcinoma of the female urethra. (Plates L and LI.) (A. J. Tiltman.) *J. Pathol.* 1975, **117**, 97.

Leiomyoma of the female urethra. (D. B. Smith *et al.*) *J. Arkansas Med. Soc.* 1975, **72**, 203.

Primary carcinoid tumor of urethra. (H. O. Sylora *et al.*) *J. Urol.* 1975, **114**, 150.

Investigatory Procedures. Reflux into vagina, uterus, fallopian tubes and peritoneal cavity during voiding cystourethrography: case report. (P. R. Bolich and D. P. Babbitt.) *Pediatr. Radiol.* 1975, **3**, 242.

Operative Procedures. Cholesterol emboli in transurethral curettings: report of 4 cases. (T. C. Knechtges and B. A. Defever.) *J. Urol.* 1975, **114**, 102.

Abdominal urethropexy; vesicourethrolysis vs Marshall-Marchetti-Kranz procedure. (P. E. Callaghan.) *South. Med. J.* 1975, **68**, 1231.

Representation of changes in condition of female urethra relative to Wick urethrocystocolporectography. (H. J. Kumper *et al.*) *Zentralbl. Gynaekol.* 1975, **97**, 1217.

Transurethral sphincterotomy: relationship of site of incision to post-operative potency and delayed hemorrhage. (M. D. Kiviat.) *J. Urol.* 1975, **114**, 399.

Segmental urethrectomy and urethrorrhaphy for treatment of fresh and late traumatic urethral lesions. (C. Chatelain *et al.*) *Eur. Urol.* 1975, **1**, 126.

Transurethral resection for the assessment and treatment of vesical neoplasms. A review of 840 consecutive cases. (J. D. O'Flynn *et al.*) *Eur. Urol.* 1975, **1**, 38.

Another look at Pereyra's steat urethropexy. (M. L. Duggan.) *South. Med. J.* 1975, **68**, 1381.

MICTURITION

General. Standardization recommendation for micturition cystourethrography in childhood. (G. Godicke *et al.*) *Radiol. Diagn.* 1975, **16**, 305.

Physiology. State of sphincteric occlusion apparatus after rectal operations for incontinence. (J. Wedell and K. Griesenbeck.) *Zentralbl. Chir.* 1975, **100**, 985.

Comparative study of sacral medullary stimulation and stimulation of detrusor urinae in dog. (U. Jonas *et al.*) *J. Urol. Néphrol.* 1974, **80**, 293.

The structure and innervation of smooth muscle in the wall of the bladder neck and proximal urethra. (J. A. Gosling and J. S. Dixon.) *Br. J. Urol.* 1975, **47**, 549.

Dynamic and pharmacologic urethral pressure profile study: significance of α-adrenergic role in the sphincteric urethra. (T. Koyanagi.) *Jpn. J. Urol.* 1975, **66**, 632.

Innervation of posterior urethra and cervix vesicae. (G. Vernet.) *J. Urol. Néphrol.* 1974, **80**, 183.

Investigatory Procedures. Electromyography of detrusor muscle. (P. T. Doyle *et al.*) *J. Urol.* 1975, **114**, 208.

Mechanism in closure of the internal urethral orifice during ejaculation. (Y. Kimura *et al.*) *Urol. Int.* 1975, **30**, 341.

Simultaneous urethrocystometry and urethra pressure profile measurement with a new technique. (M. Asmussen and U. Ulmsten.) *Acta Obstet. Gynecol. Scand.* 1975, **54**, 385.

Electrical exploration of urethral and anal sphincter muscles. (A. Chantraine.) *J. Urol. Néphrol.* 1974, **80**, 207.

In-vivo determination of error in the measurement of urethral pressure by the method of Brown and Wickham. (M. Brown.) *Br. J. Urol.* 1975, **47**, 445.

A method for recording intraluminal urine flow (application of ultrasonic doppler technique). (S. Tsuchida *et al.*) *Jpn. J. Urol.* 1975, **66**, 781.

Role of uroflowmetry in the assessment of lower urinary tract obstruction in adult males. (I. Shoukry *et al.*) *Br. J. Urol.* 1975, **47**, 559.

Measurement of the volume of residual urine using ^{131}I-hippuran and the gamma camera. (E. Kalis *et al.*) *Br. J. Urol.* 1975, **47**, 567.

Reproducibility of urine flow curves. (D. Dutartre and J. G. Susset.) *J. Urol. Néphrol.* 1974, **80**, 484.

Local Disorders. Dialogue à propos de . . . rétention aiguë d'urines. (M. le Guillou.) *Rev. Prat.* 1975, **25**, 3776.

Urinary retention due to ritual circumcision. (W. Berman.) *Pediatrics*, 1975, **56**, 621.

Herpes zoster induced urinary retention in Hodgkin's disease. (M. S. Shaukat.) *Am. J. Med. Sci.* 1975, **269**, 399.

Non-parasitic chyluria (presenting with urinary retention). (T. V. Taylor *et al.*) *Br. J. Urol.* 1975, **47**, 419.

Intravaginal and intrauterine refluxing of urine in children: intravaginal refluxing of urine in women: some postulates arising from these findings. (G. Beale.) *Australas. Radiol.* 1975, **19**, 194.

Neurogenic Disorders. Problems associated with the use of external urinary collectors in the male paraplegic. (J. B. Nanninga and J. Rosen.) *Paraplegia*, 1975, **13**, 56.

Urinary problems posed by flaccid paralysis of perineal muscles. (F. Jurascheck *et al.*) *J. Urol. Néphrol.* 1974, **80**, 298.

Dysuria in acquired paraplegia of adults following medullary shock. (J. Cukier.) *J. Urol. Néphrol.* 1974, **80**, 251.

Problems posed by spasticity in general and in urology. (P. Lacert and A. Grossiord.) *J. Urol. Néphrol.* 1974, **80**, 271.

Experience with intermittent catheterization in chronic spinal cord injury patients. (C. F. Firlit *et al.*) *J. Urol.* 1975, **114**, 234.

Urinary catheterization in severe sphincter spasticity: report of two cases. (B. M. Gans *et al.*) *Arch. Phys. Med. Rehabil.* 1975, **56**, 498.

Neuropathic bladder in childhood—urinary diversion or conservative treatment. (K. Stockamp.) *J. Urol. Néphrol.* 1974, **80**, 295.

Bladder-neck resection in multiple sclerosis—surgical aspects. (B. E. Jakobsen.) *J. Urol. Néphrol.* 1974, **80**, 337.

The autonomic nervous system and the bladder during spinal shock—an experimental study. (A. G. S. Tulloch and A. B. Rossier.) *Paraplegia*, 1975, **13**, 42.

Urinary incontinence in paraplegics and tetraplegics. (N. Francois *et al.*) *J. Urol. Néphrol.* 1974, **80**, 267.

Bladder viscerovascular reflux in cerebral lesions. (L. Timmermans.) *J. Urol. Néphrol.* 1974, **80**, 229.

Treatment of urinary bladder paralysis with small calibre suprapubic drainage. (J. B. Cook and P. H. Smith.) *J. Urol. Néphrol.* 1974, **80**, 245.

Urethral pressure measurement after division of the external sphincter. (B. J. Abel *et al.*) *Paraplegia*, 1975, **13**, 37.

Surgical treatment of dysuria in paraplegic patients involving cervix vesicae, prostate gland and sphincter muscles. (J. Vacant *et al.*) *J. Urol. Néphrol.* 1974, **80**, 258.

Intermittent catheterization and bladder rehabilitation in spinal cord injury patients. (I. Perkash.) *J. Urol.* 1975, **114**, 230.

Cutaneous ureteroileostomy in spinal cord injured patient: 15-year experience. (I. Koziol and R. H. Hackler.) *J. Urol.* 1975, **114**, 709.

Bladder and rectum disturbances in multiple sclerosis patients. (E. Schneider.) *Schweiz. Arch. Neurol. Neurochir. Psychiatr.* 1975, **116**, 301.

Long-term results of sacral rhizotomy for ureteral reflux in the spinal cord injured. (E. L. Cashion and B. A. Moeller.) *Paraplegia*, 1975, **13**, 153.

Bladder training: its role in evaluating the effect of an antispasticity drug on voiding in patients with neurogenic bladder. (M. S. Roussan *et al.*) *Arch. Phys. Med. Rehabil.* 1975, **56**, 463.

Importance of urostatic and urodynamic research methods for classification of neurogenic disorders of bladder. (C. Frimodtmoller *et al.*) *J. Urol. Néphrol.* 1974, **80**, 213.

Reflux in neurogenic bladder of myelomeningocele—discussion on importance of antireflux interventions. (J. P. Deburge *et al.*) *J. Urol. Néphrol.* 1974, **80**, 331.

Neurological mechanism of urination. (S. Gilvernet.) *J. Urol. Néphrol.* 1974, **80**, 419.

Neurological disorders of bladder and its sphincter muscles—reporters conclusions. *J. Urol. Néphrol.* 1974, **80**, 344.

Neurogenic bladder in extrapyramidal syndromes. (L. Quenu.) *J. Urol. Néphrol.* 1974, **80**, 341.

Neurogenic bladder—supravesical urinary excretion or medical treatment. (K. Stockamp and R. Hohenfellower.) *J. Urol. Néphrol.* 1974, **80**, 331.

Medullary neurostimulation of neurogenic bladder. (J. P. Sarramon *et al.*) *J. Urol. Néphrol.* 1974, **80**, 287.

Urinary derivations in neurogenic bladder. (D. Beurton *et al.*) *J. Urol. Néphrol.* 1974, **80**, 302.

Neurologic bladder in cases of sacrococcygeal agenesis. (A. Tramoyerescases *et al.*) *J. Urol. Néphrol.* 1974, **80**, 329.

Electronic stimulations in neurogenic bladder. (E. Debacker.) *J. Urol. Néphrol.* 1974, **80**, 284.

Value of functional cystography with ice cold contrast medium and urodynamic study of supranuclear neurogenic bladder. (F. Solebalcells *et al.*) *J. Urol. Néphrol.* 1974, **80**, 224.

Radiological exploration of neurogenic bladder. (A. Pinet.) *J. Urol. Néphrol.* 1974, **80**, 199.

Urodynamic study on neurogenic bladder. (F. Solebalcells *et al.*) *J. Urol. Néphrol.* 1974, **80**, 219.

Rehabilitation of paraplegic patients: the problems involved in urinary retraining of neurological bladders. (M. Forgerit *et al.*) *Ouest. Med.* 1975, **28**, 1187.

Present indications for stimulation of the spinal cord in neurogenic bladder. (J. P. Sarramon *et al.*) *J. Urol. Néphrol.* 1975, **81**, 599.

The effect of an antibacterial drug on urinary calcium, magnesium and phosphorus excretion in patients with neurogenic bladder. (R. G. Burr and J. R. Silver.) *Br. J. Urol.* 1975, **47**, 425.

Silent neurogenic bladder. (J. G. Bucy and M. R. Carlin.) *J. Urol.* 1975, **114**, 296.

Functional training of the "post-traumatic neurological bladder". (P. Boissinot *et al.*) *Ouest Méd.* 1975, **28**, 977.

Function of ureter in neurogenic bladder. (H. Melchior.) *J. Urol. Néphrol.* 1974, **80**, 447.

Incontinence Treatment. Stress incontinence in the woman. (M. Ziegler and K. Haubensak.) *Langenbecks Arch. Chir.* 1975, **339**, 447.

Treatment of post-prostatectomy urinary incontinence with heterologous bone implant. (P. Nummi.) *Ann. Chir. Gynaecol. Fenn.* 1975, **64**, 307.

Treatment of urinary incontinence by the Scott-Bradley-Timm artificial sphincter. A report of eight cases. (T. Hald *et al.*) *Urol. Res.* 1975, **3**, 133.

Stress incontinence in women—surgical treatment. (L. Lafrance.) *J. Urol. Néphrol.* 1974, **80**, 470.

Multiple etiology of stress incontinence. (J. G. Susset and A. Leriche.) *J. Urol. Néphrol.* 1974, **80**, 480.

Reflex electrical stimulation for urinary incontinence. (S. Rakovec.) *Eur. Urol.* 1975, **1**, 24.

Urinary incontinence on effort in women. (F.

Ponstonnier and J. P. Sarramon.) *J. Urol. Néphrol.* 1975, **81**, 592.

Value of colpocystography for diagnosing incontinence. Report on experiences. (W. Fischer *et al.*) *Zentralbl. Gynaekol.* 1975, **97**, 1224.

Influence of electric acupuncture on closing mechanism of female urethra in cases of stress incontinence. (E. Kubista *et al.*) *Geburtshilfe. Frauenheilkd.* 1975, **35**, 705.

Results of the treatment of post-operative urinary incontinence in man by Kaufman prosthesis. (L. Boccon-Gibod *et al.*) *Ann. Urol.* 1975, **9**, 155.

Notes on surgical technique in the correction of urinary incontinence under effort. (F. Cappello and T. D'Amato.) *Minerva Ginecol.* 1975, **27**, 722.

Use of implantable prostheses for treatment of urinary incontinence and impotence. (J. J. Kaufman and S. Raz.) *Am. J. Surg.* 1975, **130**, 244.

Treatment of urinary incontinence in women using intravaginal tarsette. (L. G. Endsley *et al.*) *J. Urol.* 1975, **114**, 50.

The importance of clinical and radiological evaluation in the choice of correct surgical management in urinary stress incontinence. (S. M. Rubino.) *Minerva Ginecol.* 1975, **27**, 579.

Enuresis. Primary enuresis: relative success of three methods of treatment. (J. B. J. McKendry *et al.*) *Can. Med. Assoc. J.* 1975, **113**, 953.

Understanding and managing enuresis in children. (S. J. Arnold and A. Ginsburg.) *Postgrad. Med.* 1975, **58**, 73.

Enuresis. (M. W. Cohen.) *Pediatr. Clin. N. Am.* 1975, **22**, 545.

The urodynamic assessment of adult enuresis. (M. J. Torrens and C. D. Collins.) *Br. J. Urol.* 1975, **47**, 433.

URINARY DIVERSION

Ileal conduit in pelvic cancer patients. (S. Sagawa *et al.*) *Jpn. J. Urol.* 1975, **66**, 785.

Urinary tract reconstruction following ileal-conduit and colonic-conduit in children. (G. Montfort.) *Aktuel. Urol.* 1975, **6**, 147.

Pain relief by percutaneous cervical cordotomy in urological patients. (K. Fleischmann and H. Wandt.) *Urologe*, 1975, **14**, 243.

Spiral advancement skin flap for stomal revision. (A. D. Perlmutter.) *J. Urol.* 1975, **114**, 131.

Ileal conduit parastomal hernias. (F. F. Marshall *et al.*) *J. Urol.* 1975, **114**, 40.

Add-on ileal loop. (P. Poor *et al.*) *J. Urol.* 1975, **114**, 281.

Reconstruction of previously diverted urinary tract in children. (M. Carcassonne *et al.*) *J. Pediatr. Surg.* 1975, **10**, 741.

The value of intestinal valves in urinary diversion—an experimental study. (A. J. S. Knox and R. H. Jago.) *Br. J. Urol.* 1975, **47**, 391.

Ileal conduit urinary diversion in children. (R. Rabinowitz and S. E. Price.) *J. Urol.* 1975, **114**, 444.

13-year experience with ileal loop diversion in children with myelodysplasia. (R. C. Flanigan *et al.*) *Am. J. Surg.* 1975, **130**, 535.

Urinary diversion through isolated bowel segments. (P. Strohmenger and G. Kierfeld.) *Langenbecks Arch. Chir.* 1975, **340**, 91.

Fate of 90 children with ileal conduit urinary diversion decade later: analysis of complications, pyelography, renal function and bacteriology. (S. R. Shapiro *et al.*) *J. Urol.* 1975, **114**, 289.

Ileal conduit urinary diversion in children: computer analysis of followup from 2 to 16 years. (G. R. Schwarz and R. D. Jeffs.) *J. Urol.* 1975, **114**, 285.

Ileal conduit—jejunal fistula following cystectomy and urinary diversion. (S. Kumar and H. Grabstald.) *J. Urol.* 1975, **114**, 466.

Continent ileal bladder. An experimental study in dogs. (H. J. Leisinger *et al.*) *Eur. Urol.* 1975, **1**, 103.

Urologic management of the traumatic cord bladder. (A. E. Comarr.) *Clin. Orthop.* 1975, **112**, 53.

Endoscopy of ureterointestinal conduits and retrograde pyelography. (D. B. Falkenstein *et al.*) *Gastrointest. Endosc.* 1975, **22**, 24.

Papillary (transitional) carcinoma in ileal conduit. (O. G. Banigo *et al.*) *J. Urol.* 1975, **114**, 626.

Pressure measurements in ileal conduits. (R. M. Weiss *et al.*) *J. Urol.* 1975, **114**, 591.

LITHIASIS (in General)

Fasting uric acid and phosphate in urine and plasma of renal calcium stone formers. (P. Schwille *et al.*) *Nephron*, 1975, **16**, 116.

Pathophysiology and therapy of hypercalciuria in patients who form recurrent stones. (E. Ritz *et al.*) *Eur. Urol.* 1975, **1**, 131.

Experimental urinary stone formation following persorption. (A. Rost *et al.*) *Eur. Urol.* 1975, **1**, 151.

Trends in calcium stone research. (J. M. Baumann.) *Urol. Res.* 1975, **3**, 103.

Microscopic investigation of the partial stages of dissolution processes in urinary calculi. (H. H. Seyfarth *et al.*) *Münch. Med. Wochenschr.* 1975, **117**, 1841.

The experimental and clinical studies on the urinary calculi with special reference to the metabolism of uric acid, 1, 2 & 3. (T. Kawamura.) *Jpn. J. Urol.* 1975, **66**, 656, 661, 672.

Stone season. 10-year retrospective study of 768 surgical stone cases with respect to seasonal variation. (J. P. Elliott *et al.*) *J. Urol.* 1975, **114**, 574.

On the problem of lysozymuria in urolithiasis. (Th. Herrmann *et al.*) *Dtsch. Gesundh.* 1975, **30**, 1408.

Recurrent urolithiasis during childhood. (L. Vendl.) *Urologe*, 1975, **14**, 164.

Microstructure of urinary tract stone formations. (W. M. Bausch and G. Sorger.) *Urologe*, 1975, **14**, 161.

Urolithiasis during childhood. (L. Vendl.) *Urologe*, 1975, **14**, 168.

Urine stones symposium CSSR-DDR in Marianske Lazne, 1974, 4th June, Urine stone symposium. (H. J. Schneider.) *Urologe*, 1975, **14**, 205.

Cystine stone therapy with mercapto-propyonyl-glycine (MPG) (thiola). (B. Terhorst and H. W. Stuhlsatz.) *Urologe*, 1975, **14**, 190.

Biliary and urinary calculli—pathogenesis following small bowel bypass for obesity. (L. Wise and T. Stein.) *Arch. Surg.* 1975, **110**, 1043.

URINARY TRACT INFECTIONS

Experimental research on endotoxic shock in urology. (C. Blaja and A. Popescu.) *Eur. Urol.* 1975, **1**, 101.

Management of urinary tract infections. (N. B.

Hodgson and J. P. Walsh.) *Surg. Clin. North Am.* 1975, **55**, 1397.

Urine sediment as an indicator of urinary tract infection. (M. J. Bennett and R. C. McCormack.) *Va. Med. Month.* 1975, **102**, 952.

Urinary tract infection following voiding cystourethrography. (J. P. Guignard *et al.*) *Schweiz. Med. Wochenschr.* 1975, **105**, 1654.

Etiology and therapy of recurrent urinary tract infection and enuresis in girls. (R. Harzmann and R. Chiari.) *Urol. Int.* 1975, **30**, 455.

Urinary infection and prostatectomy. (F. R. Jackaman and G. D. Chisholm.) *Br. J. Urol.* 1975, **47**, 545.

Urinary tract infection and wound infection in kidney transplant patients. (S. Walter *et al.*) *Br. J. Urol.* 1975, **47**, 513.

Pyelo-ureteritis cystica associated with a urinary tract infection due to a coagulase-negative staphylococcus. (L. J. Barrat and A. H. Slavotinek.) *Aust. N.Z. J. Med.* 1975, **5**, 447.

Influence of hormone contraceptives on frequency of urinary tract infections. (E. Magdowski.) *Zentralbl. Gynaekol.* 1975, **97**, 1268.

Evaluation of antibody coating of yeasts in urine as an indicator of the site of urinary tract infection. (S. A. Harding and W. G. Merz.) *J. Clin. Microbiol.* 1975, **2**, 222.

Long-term treatment with methenamine hippurate in recurrent urinary tract infection. (S. Nilsson.) *Acta Med. Scand.* 1975, **198**, 81.

Childhood urinary infection associated with vesicoureteric reflux. (M. E. MacGregor and P. Freeman.) *Q. J. Med.* 1975, **41**, 481.

Long-term urinary tract infections. (C. M. Kunin.) *Ann. Intern. Med.* 1975, **83**, 273.

Carbenicillin therapy of urinary tract infections due to difficult uropathogens-introduction. (W. J. Holloway.) *Curr. Ther. Res.* 1975, **18**, 229.

The justification for early radiological investigations of urinary-tract infection in children. (S. R. Saxena *et al.*) *Lancet*, 1975, **2**, 403.

Studies of introital colonization in women with recurrent urinary infections. 1. Role of vaginal pH. (T. A. Stamey and M. M. Timothy.) 2. Comparison of growth in normal vaginal fluid of common versus uncommon serogroups of *Escherichia coli*. (T. A. Stamey and M. F. Kaufmann.) 3. Vaginal glycogen concentrations. (T. A. Stamey and M. M. Timothy.) *J. Urol.* 1975, **114**, 261, 264, 268.

TUMOURS (in General)

Chemotherapy of urologic cancer. (S. K. Carter, and T. H. Wasserman.) *Cancer*, 1975, **36**, 729.

Characteristics of the tumours of the urinary tract in patients with endemic nephropathy. (N. Atanassov and I. Donovski.) *Eur. Urol.* 1975, **1**, 26.

Preliminary evaluation of VM-26. A new epipodophyllotoxin derivative, in the treatment of urogenital tumours. (M. Pavone-Macaluso *et al.*) *Eur. Urol.* 1975, **1**, 53.

A unique presentation of malignant tumours of the urogenital tract. (N. H. Moharib.) *Br. J. Urol.* 1975, **47**, 578.

CYTOLOGY

False cytodiagnosis of bladder malignancy due to previous radiotherapy. (P. N. Cowen.) *Br. J. Urol.* 1975, **47**, 405.

RADIOLOGY—ISOTOPE STUDIES—SONOGRAPHY

Review of 100 renal and perinephric sonograms with anatomic diagnoses. (W. R. Pitts *et al.*) *J. Urol.* 1975, **114**, 21.

Transrectal ultrasonotomography of prostate. (H. Watanabe *et al.*) *J. Urol.* 1975, **114**, 734.

Lymphocyst: ultrasound diagnosis and urologic management. (G. T. Basinger and R. F. Gittes.) *J. Urol.* 1975, **114**, 740.

Association of cystomanometry with radiological and radioisotope techniques. (L. Timmermans and M. Collard.) *J. Urol. Néphrol.* 1974, **80**, 202.

Dynamic study of urinary bladder using ^{99m}Tc-(Sn)-DTPA and γ-scintillation camera (preliminary report). (Y. Nishikage *et al.*) *Jpn. J. Urol.* 1975, **66**, 770.

Clinical value of sequential renal scans with iodo-^{131}Hippuran and renal perfusion with Tc-99m compounds using computer analysis. (E. Hecking *et al.*) *Fortschr. Geb. Roentgenstr. Nuklearmed.* 1975, **123**, 103.

Isotope nephrographic investigations after experimental unilateral fractionated irradiation of a kidney. (R. Voigt *et al.*) *Fortschr. Geb. Roentgenstr. Nuklearmed.* 1975, **123**, 113.

Determination of individual J-131-hippurate-clearance in ptotic kidneys combined with sequential scintigraphy (Gammacamera). (B. Leisner *et al.*) *Nucl. Med.* 1975, **14**, 125.

Angioscintiphotography with Tc-99 in 310 cases of space-occupying kidney lesions. (G. Tori *et al.*) *Nucl. Med.* 1975, **14**, 133.

SEMINAL VESICLE

Unusual conditions simulating ectopic ureterocele—unilateral hydrometrocolpos with ipsilateral renal agenesis or hypoplasia and ectopic ureteral opening into a seminal vesicle. (T. J. Sutton and N. Gauthier.) *Radiology*, 1975, **117**, 381.

Opening of the ureter into the seminal vesicle and carcinoma of the testis. (D. Lange.) *J. Urol. Nephrol.* 1975, **81**, 602.

VAS DEFERENS

Vasectomy. Triorchidism with normal spermatogenesis, an unusual cause of failure of vasectomy. (M. Hakami and S. H. Mosavy.) *Br. J. Surg.* 1975, **62**, 633.

Semen zinc levels in infertile and postvasectomy patients and patients with prostatitis. (J. L. Marmar *et al.*) *Fertil. Steril.* 1975, **26**, 1057.

Advances in understanding the effects of vasectomy. (J. E. Davis and I. Lubell.) *Mt. Sinai J. Med. N.Y.* 1975 **42**, 391.

Effect of irrigation of vas deferens on sperm analyses after vasectomy. (T. Lehtonen.) *Ann. Chir. Gynaecol. Fenn.* 1975, **64**, 224.

Vasectomy program at Ramathibodi Hospital—training, research and public education. (V. Muangmun *et al.*) *J. Med. Assoc. Thai.* 1975, **58**, 455.

Two year's experience of an outpatient vasectomy service. (A. J. Sobrero and K. L. Kohli.) *Am. J. Public Health*, 1975, **65**, 1091.

A reversible method of vasectomy. (J. Frick.) *Contraception*, 1975, **12**, 125.

The effects of vasectomy on spermatogenesis in the dog, *Canis familiaris*: a meiotic analysis. (M. K. MacDougall *et al.*) *Fertil. Steril.* 1975, **26**, 786.

Autoantibody formation following voluntary vasectomy. (W. B. Schill *et al.*) *Urologe*, 1975, **14**, 194.

Lymphocytotoxins in vasectomised men. (A. G. White *et al.*) *J. Urol.* 1975, **114**, 240.

EPIDIDYMIS

Primary leiomyosarcoma of epididymis. (K. C. Davides *et al.*) *J. Urol.* 1975, **114**, 642.

Solitary epididymal schistosomiasis. (L. H. Honoré and G. U. Coleman.) *Can. J. Surg.* 1975, **18**, 479.

Studies on the physiology of the human epididymis and vas deferens. 1. Biochemical constituents. (M. Rajalakshmi *et al.*) *Contraception*, 1975, **12**, 175.

Comparison of results of treatment of hydrocele and epididymal cysts by surgery and injection. (G. E. Moloney.) *Br. Med. J.* 1975, **3**, 478.

Bilateral fibrosarcoma of the epididymis. (M. McCormack.) *J. Clin. Pathol.* 1975, **28**, 576.

TESTIS

General. Cysts of tunica albuginea. Report of 4 cases and review of literature. (R. Mancilla-Jimenez and G. T. Matsuda.) *J. Urol.* 1975, **114**, 730.

Simple cyst of the testis: case report and review of literature. (S. E. Tosi and J. R. Richardson.) *J. Urol.* 1975, **114**, 473.

Meso-appendicular testis. (A. Zelikovski *et al.*) *Br. J. Urol.* 1975, **47**, 579.

An experimental mouse testicular teratoma as a model for neuroepithelial neoplasia and differentiation. II. Electron microscopy. (M. M. Herman *et al.*) *Am. J. Pathol.* 1975, **81**, 421.

An analysis of the effect of ischaemia on testicular ultrastructure (Plates LV-LXVI). M. Kaya and R. G. Harrison.) *J. Pathol.* 1975, **117**, 105.

Testicular endocrine function and cyclophosphamide in prepubertal and pubertal patients. (W. Andler *et al.*) *Helv. Paediatr. Acta*, 1975, **30**, 275.

The HCG stimulation test in men with testicular disorders. (D. M. de Kretser *et al.*) *Clin. Endocrinol.* 1975, **4**, 591.

Pattern of plasma testosterone and $\triangle^4$-androstenedione in normal newborns: evidence of testicular activity at birth. (M. G. Forest and A. M. Cathiard.) *J. Clin. Endocrinol. Metab.* 1975, **41**, 977.

A simple approach to the testis and adjacent structures. (A. L. Winniger.) *Nouv. Presse Med.* 1975, **4**, 2942.

Histology of the testes in the aging man. (R. Kaden.) *Fortschr. Med.* 1975, **93**, 1545.

Exo and endocrine testicular function in male senescence. (J. Mauss.) *Fortschr. Med.* 1975, **93**, 1543.

Emergency in testicular pathology. (F. Canavese *et al.*) *Minerva Pediatr.* 1975, **27**, 1831.

Alcohol-induced testicular atrophy. An experimental model for hypogonadism occurring in chronic alcoholic men. (D. H. van Thiel *et al.*) *Gastroenterology*, 1975, **69**, 326.

Thermoregulation of the human testis. (B. A. Lazarus and A. W. Zorgniotti.) *Fertil. Steril.* 1975, **26**, 757.

Maldescent. Two cases of perineal ectopic testis. (R. Revol *et al.*) *J. Urol. Néphrol.* 1975, **81**, 616.

Spermatogenesis following bilateral orchidopexy in adult life. (B. J. Britton.) *Br. J. Urol.* 1975, **47**, 464.

On the fertility prognosis of surgically treated dystopia of testicles. (G. Schreiber *et al.*) *Dtsch. Gesundh.* 1975, **30**, 1474.

Radiation effects on testes. VI. 5′ nucleotidase and adenosine triphosphatase following partial body gamma irradiation (English). *Radiobiol. Radiother.* 1975, **16**, 221.

Clinical aspects of a therapeutic trial involving children undergoing orchidopexy. (R. H. C. Bentall and H. B. Eckstein.) *Aktuel. Urol.* 1975, **6**, 263.

Timing of elective surgery on genitalia of male children with particular reference to undescended testes and hypospadias. (American Academy of Pediatrics.) *Pediatrics*, 1975, **56**, 497.

New views on significance and treatment of undescended testis. (L. Weissbach.) *Klin. Pädiatr.* 1975, **187**, 289.

Fetal testicular homografting for bilateral congenital anorchidism. (K. A. Hanache.) *Fertil. Steril.* 1975, **26**, 775.

Probable Xx male with hidden testes. (G. M. Lazarus and R. D. Rodner.) *J. Pediatr.* 1975, **87**, 493.

Current concepts in the management of the undescended testis. (Z. Shapira and E. Jacob.) *Harefuah*, 1975, **88**, 587.

Undescended testis: management after puberty. (D. C. Martin and H. R. Menck.) *J. Urol.* 1975, **114**, 77.

Hernia of the little boy. Undescended testicle and peritoneography. (M. Vialas.) *Pediatre*, 1975, **11**, 133.

Undescended testis: congenital or acquired? (N. A. Myers and C. B. Officer.) *Aust. Paediatr. J.* 1975, **11**, 76.

A study on cryptorchidism. 1. Changes in plasma levels of FSH, LH and testosterone in cryptorchidism with loading of luteinizing hormone-releasing hormone. (S. Matsuda.) *Jpn. J. Urol.* 1975, **66**, 462.

Androgen biosynthesis in experimental cryptorchidism. (J. C. Hoscholan and J. A. Andrada.) *Fertil. Steril.* 1975, **26**, 730.

Trauma and Torsion. A case of traumatic bilateral superficial dislocation of the testis. (K. P. Boardman.) *Injury*, 1975, **7**, 44.

Manipulation of torsion of testicle. (W. J. Frazier and J. G. Buey.) *J. Urol.* 1975, **114**, 410.

Torsion of the appendix testis. (M. Michowitz *et al.*) *Int. Surg.* 1975, **60**, 424.

Infection. Granulomatous orchitis and spermatic granuloma. (L. Kisbenedek and A. Nemeth.) *Int. Urol. Nephrol.* 1975, **7**, 141.

Neoplasms. Radiologic diagnosis of secondaries of tumors of testicle. (D. Koischwitz *et al.*) *Roentgenblatter*, 1975, **28**, 311.

Anaplastic seminoma. (D. E. Johnson *et al.*) *J. Urol.* 1975, **114**, 80.

Results of treatment for testicular tumors in children: especially on embryonal carcinoma. (T. Kawai *et al.*) *Jpn. J. Urol.* 1975, **66**, 400.

Cytostatic therapy of tumors under conditions of partial synchronisation with particular reference to malignant tumors of the testicle. (Fr. Körner *et al.*) *Münch. Med. Wochenschr.* 1975, **117**, 1345.

Incidence of yolk sac tumor (endodermal sinus tumor) elements in germ cell tumors of testis in adults. (A. Talerman.) *Cancer*, 1975, **36**, 211.

Lymphography of malignant testicular tumours. 2. Relevance determination of metastatic criteria by comparing metastatic and non-metastatic lumbar lymph-nodes. (M. Lunning *et al.*) *Radiol. Diagn.* 1975, **16**, 255.

Survival and therapeutic strategy in germinal tumors of testicle. (G. Pizzocaro *et al.*) *Tumori*, 1975, **61**, 271.

Sertoli cell tumor: case report with ultrastructural findings. (J. R. Goellner and R. P. Myers.) *Mayo Clin. Proc.* 1975, **50**, 459.

Lymphography as a guide to prognosis in malignant testicular tumours. (W. A. Fuchs and M. Girod.) *Acta Radiol.* 1975, **16**, 305.

Malignant androblastoma (Sertoli cell tumor) of testis. Case report with review of literature. (L. J. Morin and S. Loening.) *J. Urol.* 1975, **114**, 476.

Paratesticular tumours: problems of metastasis and therapy with 2 case reports. (E. Walliin *et al.*) *Ann. Urol.* 1975, **9**, 159.

Gynecomastia; interstitial cell tumor of testis as etiologic factor. (S. N. Rous and D. R. Rovner.) *N.Y. State J. Med.* 1975, **75**, 1752.

Epidermoid cyst: benign testicular tumor. (E. V. Miller.) *Int. Surg.* 1975, **60**, 487.

Endocrinology of human chorionic gonadotropin-secreting testicular tumors: new methods in diagnosis. (J. S. Cochran *et al.*) *J. Urol.* 1975, **114**, 549.

Bilateral testicular tumors of germ cell origin. (R. E. LeFevre *et al.*) *J. Urol.* 1975, **114**, 556.

Immunological studies on mouse testicular tumor. Humoral antibody response against testicular interstitial cell tumor in tumor-bearing mice. (K. Osato and F. Ikoma.) *Jpn. J. Urol.* 1975, **66**, 683.

Importance of radiological examinations for judgement on extension of malignant tumors of testicle. (E. Kuhn *et al.*) *Strahlentherapie*, 1975, **150**, 456.

Interstitial cell tumor in ectopic testicle. (F. M. Pintocoelho *et al.*) *Rev. Bras. Med.* 1975, **32**, 475.

Plasmacytoma of testis—report of a case. (D. Steinberg.) *Cancer*, 1975, **36**, 1470.

Adult teratoma of testis metastasizing as adult teratoma: case report and review of literature. (K. Kedia and E. E. Fraley.) *J. Urol.* 1975, **114**, 636.

Intratesticular leiomyoma: case report with discussion of differential diagnosis and histogenesis. (L. H. Honore and L. D. Sullivan.) *J. Urol.* 1975, **114**, 631.

Bleomycin combination chemotherapy in management of testicular neoplasia. (M. I. Samuels *et al.*) *Cancer*, 1975, **36**, 318.

Case report of embryonal rhabdomyosarcoma of testis with 8-year survival. (M. J. Jungling and D. A. Culp.) *J. Urol.* 1975, **114**, 313.

Radiotherapy for pure seminoma of the testis. (J. F. Doornbos *et al.*) *Radiology*, 1975, **116**, 401.

Germ cell testicular cancer. (P. H. Lange *et al.*) *Minn Med.* 1975, **58**, 813.

Treatment of advanced carcinoma of testis. (J. Arraztoge *et al.*) *Rev. Med. Chil.* 1975, **103**, 484.

Congenital testis embryonal carcinoma. (B. Palmieri and C. B. Silva.) *Minerva Paediatr.* 1975, **27**, 2082.

PENIS

Embryogenesis of chordee. (G. W. Kaplan and D. L. Lamm.) *J. Urol.* 1975, **114**, 769.

Devine operation in plastic induration. (F. Bianchi.) *J. Urol. Néphrol.* 1974, **80**, 421.

Evaluation of children with meatal stenosis. (H. N. Noe and G. A. Dale.) *J. Urol.* 1975, **114**, 455.

Traumatic rupture of the corpus cavernosum with report of a case belatedly treated. (J. Bauchart *et al.*) *Ann. Urol.* 1975, **9**, 81.

Balanitis xerotica obliterans in children. (D. L. McKay *et al.*) *J. Urol.* 1975, **114**, 773.

Partial amputation of the penis. (G. F. Amercrombie *et al.*) *Proc. R. Soc. Med.* 1975, **68**, 783.

Skin replacement of the penis. (H. Anderl.) *Langenbecks Arch. Chir.* 1975, **339**, 433.

Pilonidal sinus of the prepuce. (J. D. Ritchie.) *Br. J. Urol.* 1975, **47**, 580.

Webbing of the penis. (J. M. Couselosanchez *et al.*) *Rev. Esp. Pediatr.* 1975, **31**, 751.

Free autogenous grafts into the penile cavernous tissue. An experimental study in dogs. (J. Byström and K. A. Norberg.) *Urol. Res.* 1975, **3**, 145.

Parameatal cysts of glans penis: report of 9 cases. (I. W. Shiraki.) *J. Urol.* 1975, **114**, 544.

Penile prosthesis—new implant for management of impotence. (M. P. Small and H. M. Carrion.) *J. Fl. Med. Assoc.* 1975, **62**, 21.

Operative therapy of penile and scrotal elephantiasis. (F. Eisenberger and W. Keck.) *Aktuel. Urol.* 1975, **6**, 169.

Tuberculous ulcer of the penis. (V. S. Tiwari.) *Clinician*, 1975, **39**, 317.

Congenital micropenile skin sleeve. (I. W. Shiraki and R. S. Shiraki.) *J. Urol.* 1975, **114**, 469.

Surgical approach to Peyronie's disease. (L. A. Taranger *et al.*) *J. Urol.* 1975, **114**, 404.

Peyronie's disease: study of its natural history and treatment with orthovoltage radiotherapy. (W. L. Furlow *et al.*) *J. Urol.* 1975, **114**, 69.

Nonvenereal sclerosing lymphangitis of the penis. (N. J. Fiumara.) *Arch. Dermatol.* 1975, **111**, 902.

Rupture of the corpus cavernosum of the penis. (M. J. K. Hudson.) *Br. J. Clin. Pract.* 1975, **29**, 191.

4 cases of peno-scrotal avulsion. (B. Michaud and M. Rognon.) *J. Urol. Néphrol.* 1975, **81**, 558.

Tumors of the penis. (J. Brenez and R. Rettmann.) *Acta Urol. Belg.* 1975, **43**, 241.

Fifty cases of penile tumors treated at the Claude-Regaud center from 1958 to 1973. (P. F. Combes *et al.*) *J. Radiol. Electrol. Med. Nucl.* 1975, **56**, 773.

Staging carcinoma of the penis. (B. H. Baker and F. R. Watson.) *J. Surg. Oncol.* 1975, **7**, 243.

Carcinoma of the penis. (J. P. Elliott *et al.*) *J. Miss. State Med. Assoc.* 1975, **16**, 321.

Prevalence of carcinoma of the penis with special reference to India. (C. R. R. M. Reddy *et al.*) *Int. Surg.* 1975, **60**, 474.

The penis carcinoma. (J. Delsen and A. Sumoni.) *Praxis*, 1975, **64**, 1537.

Carcinoma of the penis. External beam therapy. (R. C. S. Pointon.) *Proc. R. Soc. Med.* 1975, **68**, 779.

Carcinoma of the penis external radiation mould technique. (H. Hope-Stone.) *Proc. R. Soc. Med.* 1975, **68**, 777.

Carcinoma of the penis. Surgical treatment. (J. L. Williams.) *Proc. R. Soc. Med.* 1975, **68**, 781.

Experiences with priapism. (P. J. Moloney *et al.*) *J. Urol.* 1975, **114**, 72.

Priapism. (A. Csontai *et al.*) *Acta Chir. Acad. Sci. Hung.* 1975, **16**, 7.

External shunt in treatment of idiopathic priapism. (H. W. Ten Cate *et al.*) *J. Urol.* 1975, **114**, 726.

SCROTUM

Artificial spermatocele of silicone elastomer—experimental study. (L. V. Wagenknecht *et al.*) *J. Urol. Néphrol.* 1974, **80**, 560.

Venographic demonstration of varicocele in boy. (A. Diamond and G. Ravitz.) *J. Urol.* 1975, **114**, 640.

Anazoline phosphate therapy in primary hydroceles. (J. Bodeker and R. Nagel.) *Aktuel. Urol.* 1975, **6**, 113.

Scrotal mass in a neonate—testicular abscess. (W. M. Hendricks and G. N. Kellett.) *Am. J. Dis. Child.* 1975, **129**, 1361.

Oil keratoses and scrotal cancer, an avoidable occupational dermatosis. (M. Hundeiker and V. Glossmann.) *Berufsdermatosen*, 1975, **23**, 174.

Fournier's gangrene of the scrotum. (S. Singh *et al.*) *Int. J. Dermatol.* 1975, **14**, 508.

Fournier's gangrene of the scrotum: the urologic viewpoint. (T. M. Birdsall.) *Int. J. Dermatol.* 1975, **14**, 506.

Operative management of hidradenitis suppurativa of scrotum and perineum. (M. A. Vickers.) *J. Urol.* 1975, **114**, 414.

A foreign body (chicken bone) in the rectum causing extensive perirectal and scrotal abscess: report of a case. (C. A. Moreira *et al.*) *Dis. Colon. Rectum*, 1975, **18**, 407.

Extramammary Paget's disease in scrotal and inguinal areas. (K. W. Hagan *et al.*) *J. Urol.* 1975, **114**, 154.

REPRODUCTION

Infertility. Proteolytic enzymes of semen for fertility. (W. B. Schill.) *Hautarzt*, 1975, **26**, 514.

Importance of frozen-stored human semen in the spread of gonorrhea. (J. K. Sherman and J. Rosenfeld.) *Fertil. Steril.* 1975, **26**, 1043.

Semen analysis: review of samples from 225 men seen at infertility clinic. (A. T. K. Cockett *et al.*) *J. Urol.* 1975, **114**, 560.

Creation and use of scrotal sperm bank in aplasia of vas deferens. (M. A. Vickers.) *J. Urol.* 1975, **114**, 242.

Significance of absent vas deferens at hernia repair in infants and children. (F. Lukash *et al.*) *J. Pediatr. Surg.* 1975, **10**, 765.

Male hypogonadotrophic hypogonadism. Successful treatment of infertility with HMG+HCG. (M. N. Gayral *et al.*) *Ann. Endocrinol.* 1975, **36**, 227.

Clomiphene—utilization in stimulation test and in treatment of functional sterility. (G. Goretzlehner *et al.*) *Zentralbl. Gynaekol.* 1975, **97**, 1450.

Immunologic studies of male infertility. (J. R. Wall *et al.*) *Fertil. Steril.* 1975, **26**, 1035.

Laparoscopy in the investigation of infertility. (A. N. McDougall.) *Scott. Med. J.* 1975, **20**, 209.

Varicocele and male sterility. (F. Pontonnier *et al.* *J. Urol. Néphrol.* 1975, **81**, 604.

Immunological factors in male sterility. (A. Eyquem *et al.*) *J. Gynecol. Obstet.* 1975, **4**, Suppl. 1, 93.

Seminal prostaglandins in infertile men. (J. G. Collier *et al.*) *Fertil. Steril.* 1975, **26**, 868.

Surgical laparoscopy in infertility. (M. R. Cohen.) *J. Reprod. Med.* 1975, **15**, 51.

Improvement of fertility and semen quality in men treated with a combination of anticongestive and antibiotic drugs. (T. Z. Homonnai *et al.*) *Int. J. Fertil.* 1975, **20**, 45.

Reproductive Physiology. Serum LH and FSH responses to synthetic gonadotropin-releasing hormone in normal men. (P. J. Snyder *et al.*) *J. Clin. Endocrinol. Metab.* 1975, **41**, 938.

Hormonal changes in puberty. III. Correlation of plasma dehydroepiandrosterone, testosterone FSH and LH with stages of puberty and bone age in normal boys and girls and in patients with Addison's disease or hypogonadism or with premature or late adrenarche. (P. C. Sizonenko and L. Paunier.) *J. Clin. Endocrinol. Metab.* 1975, **41**, 894.

Puberty in boys: correlation of plasma levels of gonadotropins (LH, FSH), androgens (testosterone, androstenedione, dehydroepiandrosterone and its sulfate), estrogens (estrone and estradiol) and progestins (progesterone and 17-hydroxyprogesterone). (P. A. Lee and C. J. Migeon.) *J. Clin. Endocrinol.* 1975, **41**, 556.

Human spermatogenesis. (M. Courot.) *J. Gynecol. Obstet.* 1975, **4**, suppl. 1, 1.

Effect of pharmacological agents on ejaculation. (K. Kedia and C. Markland.) *J. Urol.* 1975, **114**, 569.

Sexual function following high retroperitoneal lymphadenectomy. (K. R. Kedia *et al.*) *J. Urol.* 1975, **114**, 237.

Experimental study of electro-ejaculation in the baboon. (N. Francois *et al.*) *J. Urol. Néphrol.* 1975, **81**, 533.

Intersex. The aetiology and management of intersexuality. (C. J. Dewhurst.) *Clin. Endocrinol.* 1975, **4**, 625.

Etiologic and pathogenetic classification of male hermaphroditism. (I. J. Park *et al.*) *Am. J. Obstet. Gynecol.* 1975, **123**, 505.

Ermafroditismo vero, varietà laterale (contributo allo studio ultrastrutturale del tessuto gonadico). (F. Severi *et al.*) *Minerva Pediatr.* 1975, **27**, 1738.

Clinical and experimental aspects on abnormal sexual differentiation. (S. Mizutani.) *Jpn. J. Urol.* 1975, **66**, 545.

Preventable aspects of intersexual disorders. (V. E. Aimakhu.) *Nigerian Med. J.* 1975, **5**, 126.

Operative treatment of male pseudohermaphroditism. (P. Carl *et al.*) *Urologe*, 1975, **14**, 178.

Impotence. Impotence as a consequence of organic disease. (S. Kent.) *Geriatrics*, 1975, **30**, 155.

Clinical aspects of the impotence of male patients under regular hemodialysis treatment. (H. Loew *et al.*) *Med. Welt.* 1975, **26**, 1651.

Impotence in diabetics. (D. C. Renshaw.) *Dis. Nerv. Syst.* 1975, **36**, 369.

MISCELLANEOUS

A computer-based record and organisation system for a Department of Urology. (J. E. A. Wickham *et al.*) *Br. J. Urol.* 1975, **47**, 345.

Presentation of new double-current resector. (Iglesias.) *J. Urol. Néphrol.* 1974, **80**, 557.

Comparison between bupivacaine and etidocaine in lumbar epidural block for urological surgery. (T. Tammisto *et al.*) *Acta Anaesthesiol. Scand.* 1975, suppl. 60, 68.

Urodynamics. (H. Melchior.) *Urol. Res.* 1975, **3**, 51.

Frequency and management of urological and some other complications following radical surgery for carcinoma of the cervix uteri, stages i and ii. (T. Mattsson.) *Acta Obstet. Gynecol. Scand.* 1975, **54**, 271.

Postoperative ileus in urology. Present views, practical consequences. (G. Champault.) *Ann. Urol.* 1975, **9**, 115.

New Iglesias resectoscope. (J. J. Iglesias and U. K. Stams.) *Urologe*, 1975, **114**, 229.

Urologic cryo-surgery. (W. Lutzeyer *et al.*) *Aktuel. Chir.* 1975, **10**, 325.

Training in urology. Conclusions of the round table discussion. (A. W. Badenoch *et al.*) *Eur. Urol.* 1975, **1**, 2.

The disinfection of urological endoscopes. (J. P. Mitchell and V. G. Alder.) *Br. J. Urol.* 1975, **47**, 571.

Urinary catheterization and the catheters used. (A. Jardin and J. M. Duclos.) *Rev. Med. (Paris)*, 1975, **16**, 2616.

Using the urinary catheter and other devices. (H. Bodner.) *Postgrad. Med.* 1975, **58**, 87.

Determining the cause of hematuria. (H. G. Kudish.) *Postgrad. Med.* 1975, **58**, 118.

Leukoplakia of urinary tract: review. (R. W. Reece and W. W. Koontz.) *J. Urol.* 1975, **114**, 165.

Printed in Great Britain
by T. & A. Constable Ltd. Hopetoun Street, Edinburgh
Printers to the University of Edinburgh

INS 2

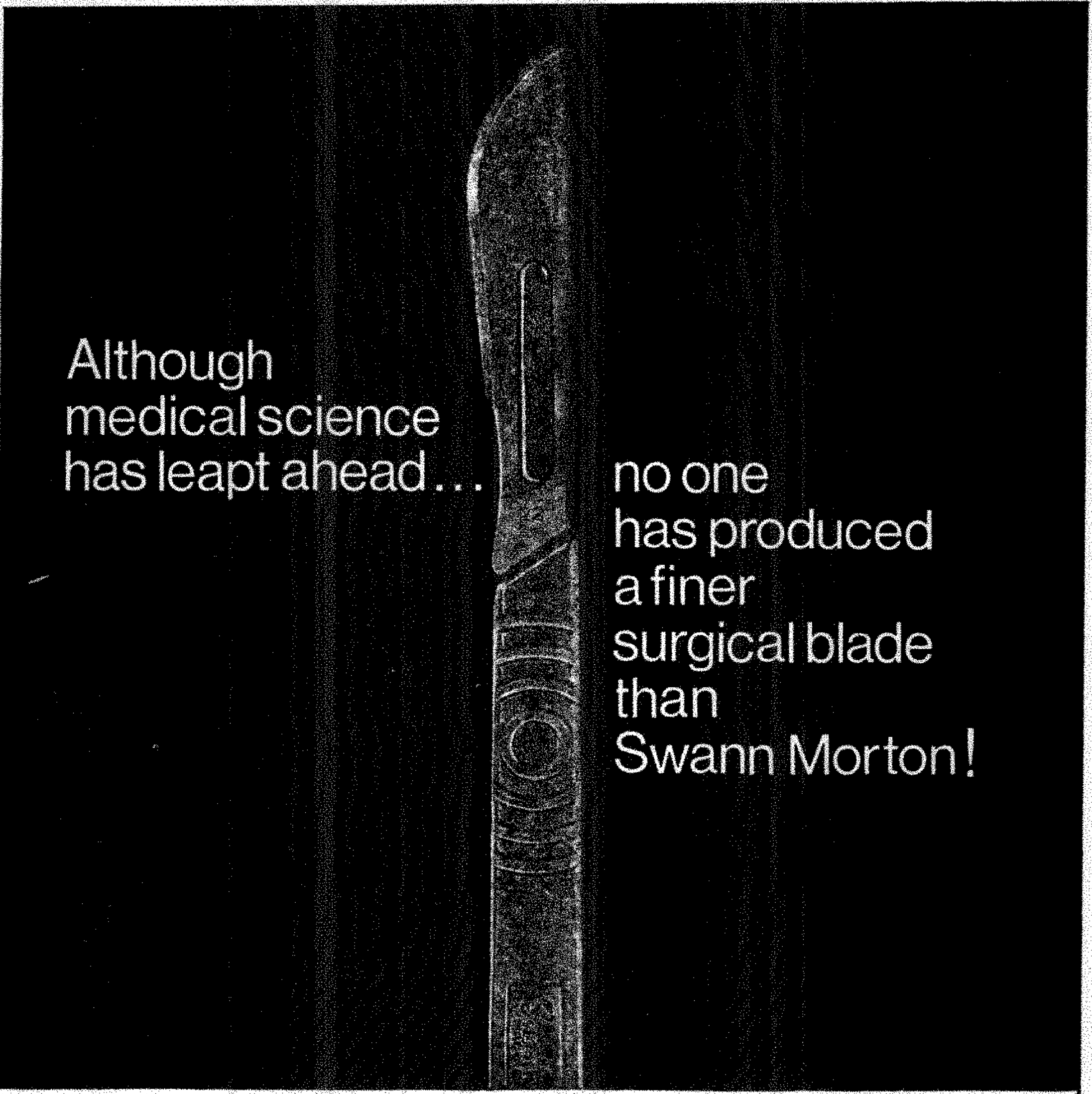
our enlarged range

. . . now offers you
a triple choice* of price
conscious, quality surgical
instruments that is hard
to match anywhere

The Medical Supply Association Ltd
Bourne Road Bexley Kent
Telephone Crayford 529114
Branches throughout the UK

*Simal, Heljestrand and MSA brands

msa instruments in a big way



Swann-Morton, the world's largest producers of surgical blades have kept abreast of the extremely high demands in surgical fields. Safe, stable and economical, their blades are sterilized by gamma radiation packed in quick peel foil envelopes and of a superb quality yet to be beaten.

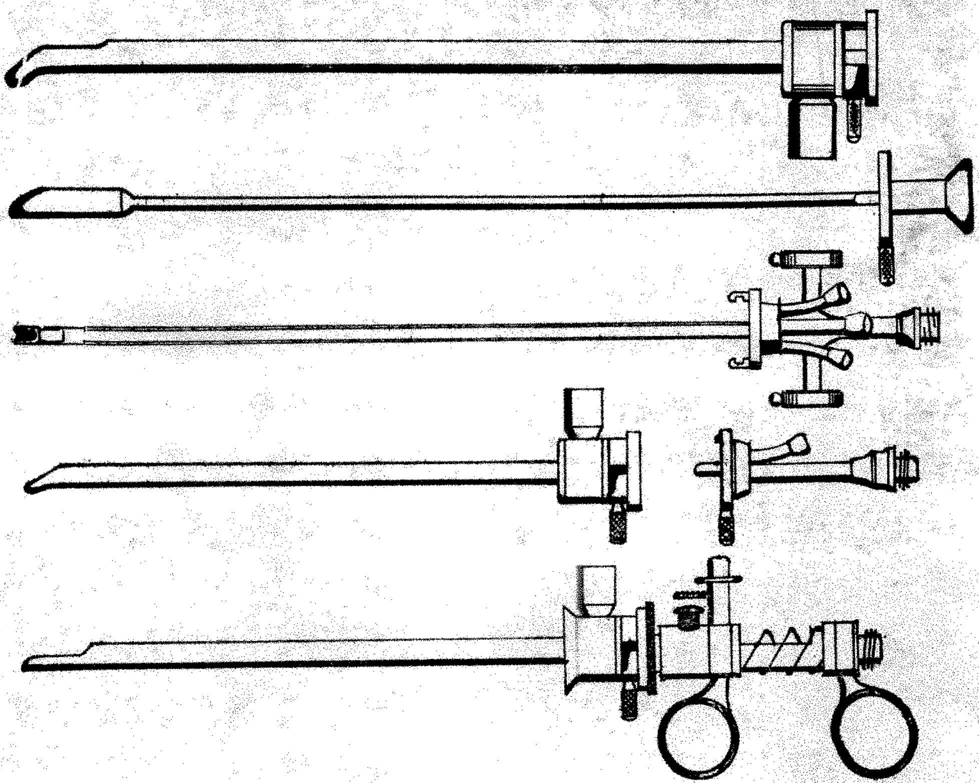
STERILIZED CARBON STEEL BLADES
STERILIZED STAINLESS STEEL BLADES
STANDARD CARBON STEEL BLADES
STERILE DISPOSABLE STITCH CUTTERS
SURGICAL HANDLES
AUTOCLAVABLE PLASTIC SURGICAL HANDLES

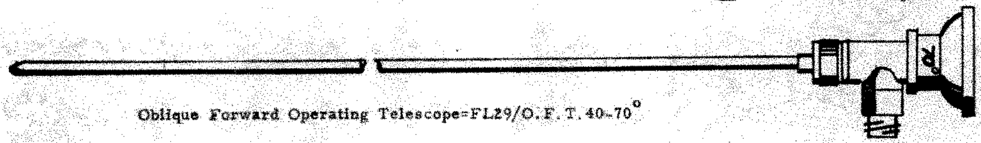
Swann-Morton

Surgical Blades

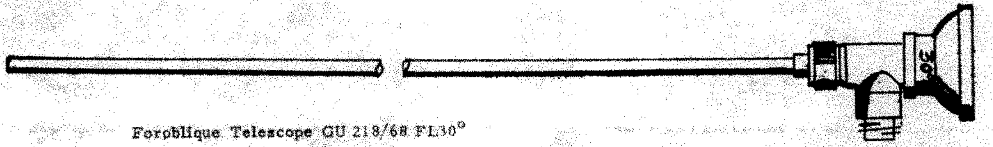
SWANN-MORTON LIMITED
PENN WORKS, OWLERTON GREEN,
SHEFFIELD S6 2BJ. ENGLAND

G.U. - BLANDY CYSTO-RESECTOSCOPE

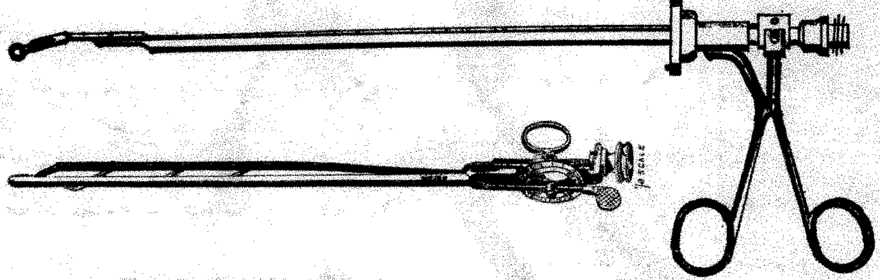




Oblique Forward Operating Telescope=FL29/O.F.T.40-70°



Foroblique Telescope GU 218/68 FL30°



Made by
THE GENITO-URINARY MANUFACTURING CO. LTD.
28a 33–34 Devonshire Street London W1N 2AJ

Telephone:
01–935 2835/6/7

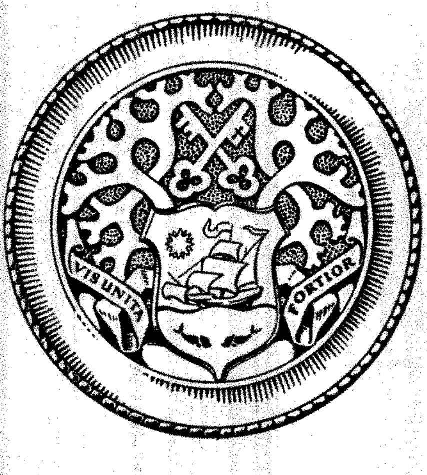
Telegrams:
Cystoscope London W1

ISSN 0007–1331

Acc.
15.11.76

BRITISH JOURNAL OF UROLOGY

Official Journal of the
British Association of Urological Surgeons



MEDICINE LIBRARY

Volume 48 No 4

August 1976

E & S Livingstone

BRITISH JOURNAL OF UROLOGY

EDITOR
* W. KEITH YEATES

HON. TREASURER
* C. H. KINDER

ASSISTANT EDITORS
* G. D. CHISHOLM
* D. M. ESSENHIGH
* W. F. HENDRY
* W. SELBY TULLOCH

ASSISTANT EDITOR FOR AUSTRALASIA
G. F. MURNAGHAN

CONSULTING EDITORS
* DAVID BAND
* J. D. FERGUSSON

EDITORIAL COMMITTEE
Chairman D. INNES WILLIAMS*

G. H. BAINES, Birmingham
JOHN BALFOUR, Vancouver
D. R. BARNES, Cape Town
J. P. BLANDY, London
JEAN CHARBONNEAU, Montreal
C. A. C. CHARLTON, Bath
PHILIP CLARK, Leeds
B. N. COLABAWALLA, Bombay
M. H. DEVEREUX, Loughton, Essex
J. N. de KLERK, Cape Town
E. CHARLTON EDWARDS, Manchester
E. J. ENGLAND, Perth, W. Australia
H. FINE, Durban
ALBAN H. GEE, Sydney
N. O. K. GIBBON, Liverpool
JOHN GRIEVE, Dundee
A. R. HARRISON, London
D. K. KARANJAVALA, Bombay
J. A. KENNEDY, Belfast
W. K. KERR, Toronto
KENNETH J. MACKINNON, Montreal
J. W. F. MACKY, Auckland
JOHN P. MADDERN, Adelaide
J. P. MITCHELL, Bristol
*RICHARD A. MOGG, Cardiff
J. DERMOT O'FLYNN, Dublin
H. H. PEARSON, M.B.E., Canberra
J. S. PETERS, Melbourne
R. C. B. PUGH, London
P. J. M. RETIEF, Cape Town
CHARLES J. ROBSON, Toronto
L. STUART SCOTT, Glasgow
K. E. D. SHUTTLEWORTH, London
SARINDER MAN SINGH, Delhi
J. C. SMITH, Oxford
J. J. STEVENSON, London
J. H. STEYN, Aberdeen
W. BARR STIRLING, Glasgow
JOHN SWINNEY, M.C., Bunbury, W. Australia
G. C. TRESIDDER, London
P. J. P. VAN BLERK, Johannesburg
DAVID M. WALLACE, O.B.E., London
J. G. WATSON, Brisbane
R. H. WHITAKER, Cambridge
*J. L. WILLIAMS, Sheffield
J. F. R. WITHYCOMBE, Cambridge

* Members of Executive Committee

ST PETER'S MEDAL AWARDED TO

J. B. MACALPINE, 1949
R. OGIER WARD, 1951
TERENCE J. MILLIN, 1951
A. CLIFFORD MORSON, 1954
LESLIE N. PYRAH, 1959
CUTHBERT E. DUKES, 1960
DAVID BAND 1962
SIR ERIC RICHES, 1964

THE BRITISH ASSOCIATION OF UROLOGICAL SURGEONS

ARTHUR H. JACOBS, 1965
D. INNES WILLIAMS, 1967
H. HAMILTON STEWART, 1968
JOHN SWINNEY, 1969
SIR MICHAEL WOODRUFF, 1970
D. S. POOLE-WILSON, 1971
DAVID M. WALLACE, 1973
A. W. BADENOCH, 1974
HOWARD G. HANLEY, 1975

E. & S. Livingstone
Edinburgh and London
August 1976

Contents

ORIGINAL ARTICLES

221 **Surgical Correction of Arterial Stenosis in Renal Allografts**
D. E. Osborn, J. E. Castro and R. Shackman

227 **Autotransplantation of the Kidney for Fibromuscular Dysplasia of the Renal Arteries**
S. G. Ball, G. R. Giles, M. S. F. McLachlan and M. R. Lee

231 **Vaginal Ureterolithotomy**
P. J. O'Boyle and N. O. K. Gibbon

235 **Preliminary Communication: The Use of Bromocriptine in the Treatment of the Unstable Bladder**
D. J. Farrar and J. L. Osborne

239 **Bladder and Urethral Innervation in Multiple Sclerosis**
Jens T. Andersen and William E. Bradley

245 **Chronic Bacterial Prostatitis: New Therapeutic Aspects**
A. Pfau and T. Sacks

255 **The Use of Alpha-adrenergic Blockers in Benign Prostatic Obstruction**
Marco Caine, Alphonse Pfau and Shaul Perlberg

265 **Random Bone Marrow Biopsy in the Staging of Carcinoma of the Prostate**
John Crisp

269 **Amoebiasis of the Penis**
John A. Thomas and A. Joseph Antony

275 **Vasoplasty: a New Technique**
V. R. Nair

279 **Comparison of Sterile Bag, Clean Catch and Suprapubic Aspiration in the Diagnosis of Urinary Infection in Early Childhood**
J. D. Hardy, P. M. Furnell and W. Brumfitt

285 **Comparison of Hydrophilic Polymer-coated Latex, Uncoated Latex and PVC Indwelling Balloon Catheters in the Prevention of Urinary Infection**
M. J. Tidd, J. G. Gow, J. H. Pennington, J. Shelton and M. R. Scott

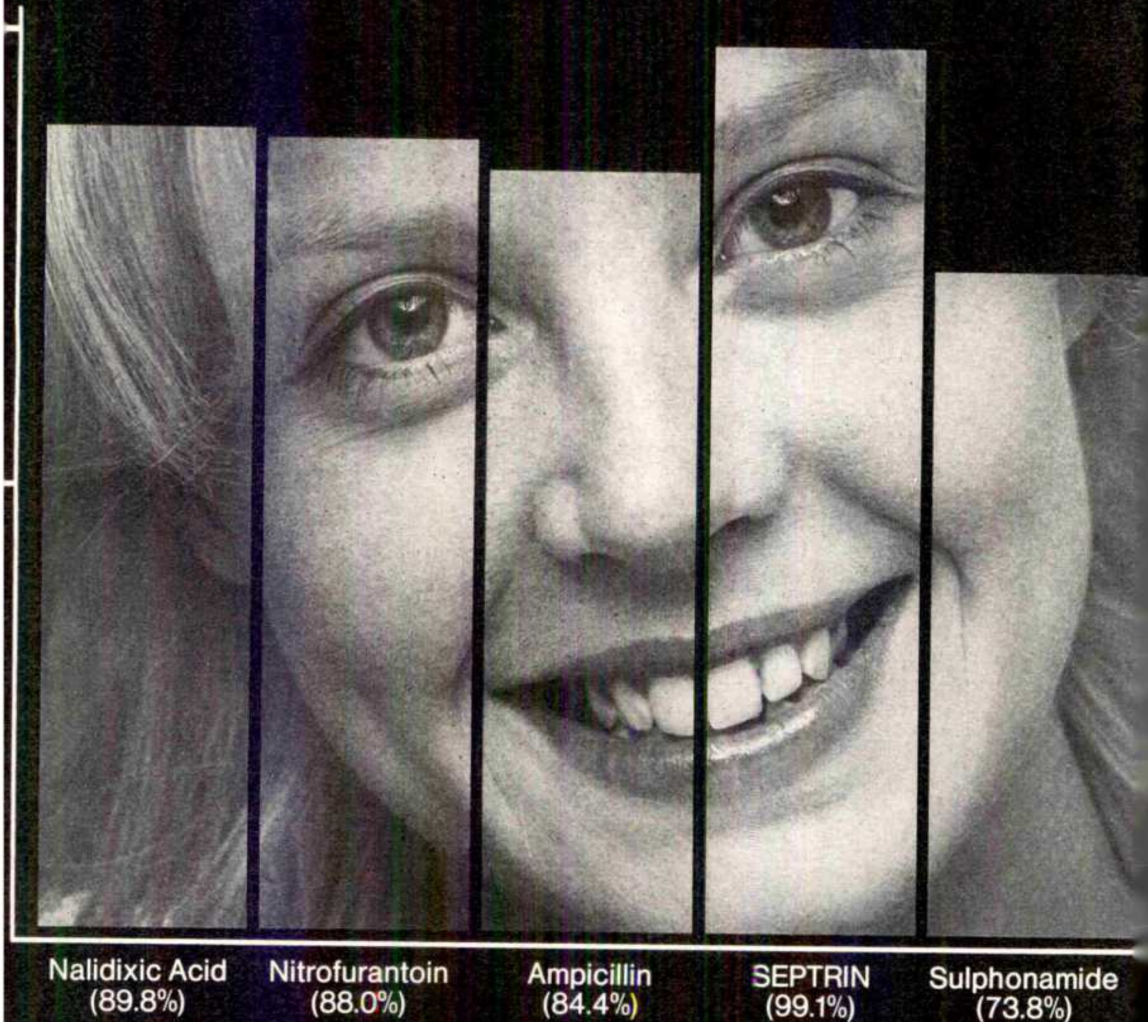
SHORT CASE REPORTS

234 **Appendix Ureteroplasty**
R. W. Weinberg

244 **Ectopia Vesicae Complicated by Squamous Cell Carcinoma**
S. Gupta and I. M. Gupta

254 **An Osteolytic Lesion as a Presentation of Bladder Carcinoma**
J. G. W. Feggetter

A 99.1% chance of success in U.T.I.



The chart above shows the percentage sensitivities of isolates from acute urinary infections against five commonly-used antibacterials. (From an *in-vitro* study involving 173 general practitioners). SEPTRIN was superior to all other oral antibacterials tested, with 99.1% of urinary pathogens sensitive

J int med Res (1974), 2, 40

come
contains
prim and
ethoxazole.
ESCRIBING
TION IS AVAILABLE
JEST.
e Medical Division
lcome Foundation Ltd
nsted Herts

SEPTRIN first

TRADE MARK

in urinary tract infectio

264 **Posterior Urethral Duplication**
D. Osborne and J. C. Gingell

268 **Regression of Penile Metastases of Prostatic Carcinoma with Cyproterone Acetate Therapy**
R. M. Jameson

274 **Tuberculosis of the Penis**
A. Sriman Narayana, D. G. Kelly and F. A. Duff

278 **Congenital Urethral Polyp in a Child**
F. H. Bagley and A. I. Davidson

284 **A Knot in the Urethra**
Wim Oosterlinck and Guy Renders

292 **Ileal Replacement of Ureter of Solitary Kidney: 22-year follow-up**
S. Wesolowski

293 BOOK REVIEWS

294 ANNOUNCEMENTS

296 ABSTRACTS FROM CURRENT UROLOGICAL LITERATURE

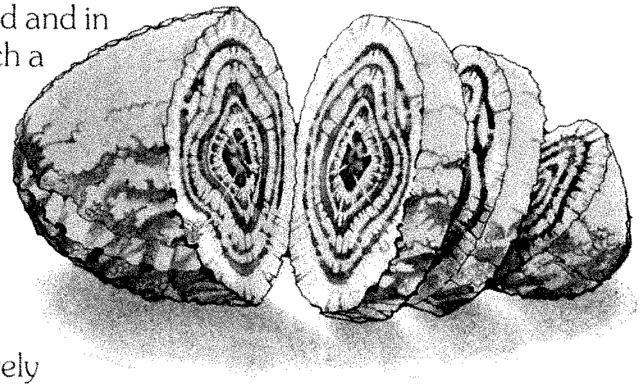
ISSN 0007-1331

Diet and renal stones. The inside story.

Traditionally, patients with idiopathic hypercalciuria have been treated with a low calcium diet.

Indeed, "A diet with a very low calcium content, less than 50mg daily, should provide an effective method of controlling calciuria."[1]

However, "due to the presence of calcium in so many kinds of food and in drinking water, such a diet is hardly possible. It is not palatable and would lack many indispensable trace elements."[1] Many foodstuffs contain a deceptively high level of calcium. A meal consisting of lamb stew can yield more calcium than the recommended allowance.[2]



This is why Whatman Sodium Cellulose Phosphate is being used increasingly as adjunctive treatment for idiopathic hypercalciuria. Whatman Sodium Cellulose Phosphate reduces calcium absorption and prevents renal stone formation.[3]

1. *Brit J Urol*, (1973), **45**, 136.
2. *Composition of Foods*, (1960), MRC Report 297, HMSO, London.
3. *American J Med*, (1971), **50**, 67.

Whatman®

Sodium Cellulose Phosphate

Fundamental treatment for idiopathic hypercalciuria.

Further information and data sheet on request from Whatman Biochemicals Limited, Springfield Mill, Maidstone, Kent ME14 2LE. Telephone: Maidstone 673841. Telex: 96113.

® Registered trade mark of Whatman Limited

0651

Instructions to Authors

The *British Journal of Urology* welcomes original contributions on urological subjects from all parts of the world. The papers are accepted for consideration on the understanding that their contents have not been published in whole or in part elsewhere and that they are subject to editorial revision.

Any paper may be sent initially to a member of the Editorial Committee for comment and advice on its being suitable to be considered for publication.

A leaflet showing the criteria used in the assessment of papers submitted for consideration is available from the Editor on request.

Authors should supply their qualifications, main appointment, and the name and address of the hospital or the laboratory.

Please indicate name and address to which requests for reprints should be made.

Format and content of papers

The text of articles submitted for publication should be typewritten in double-spacing on paper sheet size 22 × 32 cm (A4). There should be a minimum margin of 3 cm all round. The pages should be numbered.

Reports on clinical or laboratory investigation should as far as possible be organised into the following main sections: (1) Introduction, (2) Objective(s), (3) Patients or Materials, (4) Procedures or Methods, (5) Findings or Results, (6) Discussion and (7) Conclusions with (8) a Summary at the end.

Nephrology. Papers on disorders of renal function of interest to the urological surgeon are welcome.

Ethics. When relevant, authors must include a statement on the ethical aspects of their research.

Reports of clinical cases should consist of the following sections: (1) Introduction, (2) Case Reports and (3) Comment with (4) a Summary at the end.

Reports on single cases. Papers reporting a single case are considered for publication as full papers only when the case has definite instructional value. The Introduction and Discussion should not be disproportionate to the case presentation. *An abbreviated version suitable for publication as a Short Case Report as an alternative must also be submitted.*

In all full papers the literature should be summarised as concisely as is consistent with establishing the necessary basis for new material. Discussions and Conclusions should be strictly limited to the results presented. Recapitulation from previous sections should be avoided whenever possible. Summaries should be composed of very brief statements about each of the main sections.

Headings. The relative importance of sub-headings should be clearly indicated.

Numbers. All numbers should be shown as figures rather than as words.

References. *The accuracy of references is the responsibility of the author.* Only papers closely related to the author's work should be referred to; exhaustive lists should be avoided. *References in the text* should be quoted by the author's name(s) and year of publication. Unless there are more than 3 authors, all the names should be stated at the first reference; if there are more than 3 authors only the first author plus *et al.* is used. In subsequent references to the same paper, *et al.* is used if there are more than 2 authors. *The list of references at the end of the paper* should be in alphabetical order. *References to journals* should include the name(s) and initials of the author(s), year, title of paper, name of journal in full, volume number and the numbers of the first and last pages, *References to books* should include the name and initials of the author, year, title of book, number of edition, city of publication, name of publishing house, and page number(s).

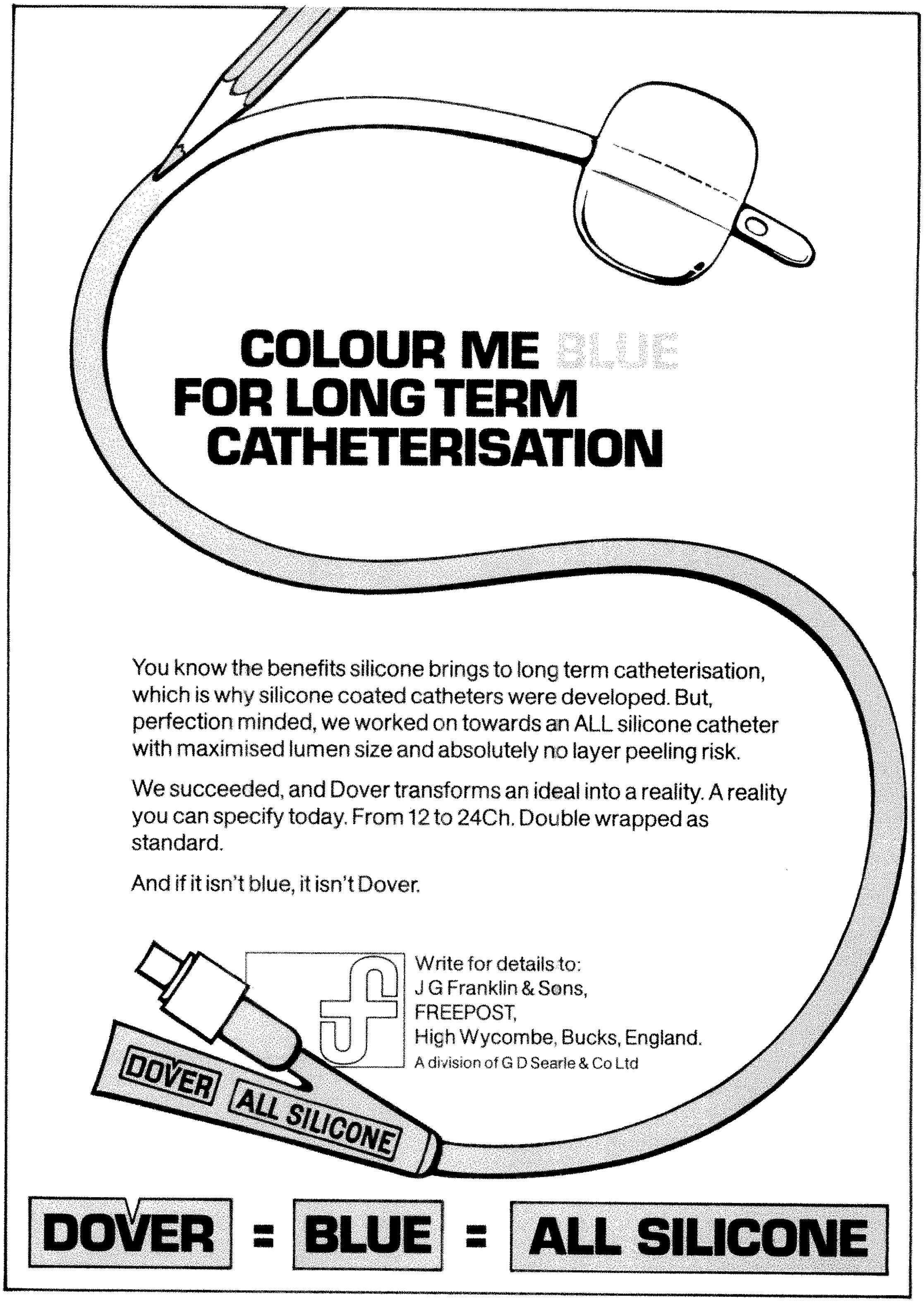
Illustrations. Photographs and radiographs should be submitted in the form of *matt* prints of a size no larger than 17·5 × 12·5 cm and no smaller than 9 × 6·5 cm. All figures should be sent unmounted. The number of the figure, the name of the author and the "top" of the illustration should be indicated lightly in pencil on the back. The magnification of micro-photographs should be stated. Graphs and diagrams should be drawn in Indian ink. *Lettering and figures must be indicated only on a transparent cover.* Legends to figures should be typewritten on a separate sheet of the manuscript. Tables, unless they are very small, should also be typewritten on separate sheets. The position of illustrations and tables should be indicated in the margin of the text.

There is no charge to contributors for the printing of black-and-white illustrations on papers accepted for publication. Illustrations in colour may be accepted at the discretion of the Editor provided he is of the opinion that these are necessary for the improvement of the article. The author may be required to pay for the extra cost involved by the reproduction in colour.

Reprints

25 offprints are supplied to the first named author only, free. Forms for ordering offprints will be sent with the proofs for correction; the order form should be returned with the corrected proofs within 7 days.

Continued on page vii



COLOUR ME BLUE
FOR LONG TERM
CATHETERISATION

You know the benefits silicone brings to long term catheterisation, which is why silicone coated catheters were developed. But, perfection minded, we worked on towards an ALL silicone catheter with maximised lumen size and absolutely no layer peeling risk.

We succeeded, and Dover transforms an ideal into a reality. A reality you can specify today. From 12 to 24Ch. Double wrapped as standard.

And if it isn't blue, it isn't Dover.

Write for details to:
J G Franklin & Sons,
FREEPOST,
High Wycombe, Bucks, England.
A division of G D Searle & Co Ltd

DOVER = BLUE = ALL SILICONE

Travelling Fellowship

The British Association of Urological Surgeons offers a Travelling Fellowship of £250 based on the best paper published in the *British Journal of Urology* in the preceding year including those papers presented at the British Association of Urological Surgeons Annual Meeting.

Candidates for the prize must be Fellows of one of the Royal Colleges of Surgeons in the British Isles, Canada, Australasia or South Africa who are in the course of urological training or who have obtained consultant posts within 10 years of the date of submission of the paper.

The Fellowship will be awarded for the best paper published in the Journal from the April issue of one year to the February issue of the following year.

Authors of papers with multiple authorship should indicate which one of their number should be awarded the Fellowship in the event of their contribution being selected.

Three assessors will be appointed by the Council to make recommendations on the award of the Fellowship. The Council reserves the right not to make an award in any one year.

The award will be announced at the June meeting of the Association.

Short Case Reports

Brief reports (preferably with 1 and not more than 2 illustrations) of unusual cases not published elsewhere may be submitted as summaries of not more than 200 words for consideration for publication as Short Case Reports. They should comprise (1) a Title, (2) Case description and (3) a brief Comment. The authors and references are each limited to 3. The titles of these reports will usually be recorded in Index Medicus and by MEDLARS.

Preliminary Communications

Preliminary communications of original work may be submitted as short papers. The communication should be divided into 4 sections: (1) Objectives, (2) Materials and Methods, (3) Preliminary results, (4) Interpretation or Significance of Results.

Discussion of Papers

Questions or criticisms concerning recently published paper may be sent to the Editor, who will refer them to the authors. The readers' comments and authors' replies may subsequently be published together.

There is no other correspondence section in the Journal.

Suggested Projects for Urological Research

Clinicians who have ideas for research projects, but have no opportunity for carrying them out, may submit them for publication in the above section. The communication should not be longer than 500 words. References will be limited to 6.

Abstracts from Current Urological Literature

Urologists who are willing to undertake abstracting of urological articles appearing in other journals should communicate with the Assistant Editor, Mr. W. Selby Tulloch, at the Department of Urology, Western General Hospital, Edinburgh, EH4 2XU.

Addresses

With the exceptions noted below, all editorial communications, including books for review, should be addressed to the Editor, Mr. W. Keith Yeates, at the Department of Urology, Newcastle General Hospital, Newcastle upon Tyne, NE4 6BE.

Preliminary Communications on Research Projects and *Suggested Projects for Urological Research* should be submitted to the Assistant Editor, Mr G. D. Chisholm, at The Urology Unit, Hammersmith Hospital, Royal Postgraduate Medical School, London, W12 0HS.

Short Case Reports (presented as described above) should be sent to the Assistant Editor, Mr W. F. Hendry, Institute of Urology, University of London, 172 Shaftesbury Avenue, London, WC2H 8JE.

Communications concerning the Abstract Section should be sent to the Assistant Editor, Mr W. Selby Tulloch, at the Department of Urology, Western General Hospital, Edinburgh, EH4 2XU.

Publishing, Advertisement and other enquiries: E. & S. Livingstone, Longman Group Ltd., Journals Division, Longman House, Burnt Mill, Harlow, Essex CM20 2JE.

Subscriptions

The Journal is published in February, April, June, August, October and December. Volume 48, number 7, is included in the subscription price and publishes the papers presented at the 1976 B.A.U.S. Conference. Subscription £17·00 (U.S.A. $45.00) per annum, post free. Single copies £3·00 (U.S.A. $9.00) each. Previous volumes and parts of volumes (if available) may be obtained from the publishers, price £6.00 per volume or 75p for single parts.

Subscription enquiries: Messrs E. & S. Livingstone, Journals Division, 43/45 Annandale Street, Edinburgh, EH7 4AT.

Subscriptions for U.S.A. should be sent to The Williams and Wilkins Company, 428 East Preston Street, Baltimore, Maryland, U.S.A.

All rights reserved. No part of this publication may be reproduced, stored in a retrieval system, or transmitted in any form or by any means, electronic, mechanical, photo-copying, recording or otherwise, without the prior permission of the copyright owner.

THACKRAY

The Raper Cystoscopy and X-ray trolley designed for all routine procedures in the Cystoscopy Clinic from examination to recovery, and for any situation where the patient is examined in the lithotomy position. Patent No. 1050834.

For further information please contact:

Valleylab

The Electrosurgery Company.

Valleylab is represented in the United Kingdom by:

ALBERT BROWNE LTD

New
Stomahesive™
Flanges!

Giving confidence in a secure appliance, maximum skin protection and the comfort of Stomahesive.

Available in sizes:
32 mm (1¼"), 38 mm (1½"), 45 mm (1¾")

A natural addition to the Stomahesive range.
Stomahesive flanges enhance the benefits of two-piece appliances.

Further information available from
E. R. SQUIBB & SONS LTD, Regal House, Twickenham TW1 3QT

SQUIBB
Stoma care

THACKRAY

System 80

A modular range for examination, catheterisation and resection. The system is built around the clarity of a rod lens telescope and manufactured to B.A.U.S. specification in accordance with patent number 954 629.

A well proven 24 hours telescope repair service is available in the U.K. when necessary.

For further information please contact: Chas. F. Thackray Limited.
Head Office: P.O. Box 171, Park Street, Leeds LS1 1RQ.

CHARLES C THOMAS • PUBLISHER

CLINICAL USE OF DRUGS IN RENAL FAILURE *by* **Robert J. Anderson,** *Univ. of Colorado, Denver;* **John G. Gambertoglio,** *Univ. of California, San Francisco; and* **Robert W. Schrier,** *Univ. of Colorado, Denver.* Patients with kidney disease generally receive more pharmacological agents than do individuals with normal kidney function. In addition to receiving more drugs, the patient with advanced renal failure may respond to a given dose of a pharmacological agent with respect to efficacy and adverse effects in a substantially different manner than the subject with healthy kidneys. This book examines these and other important considerations in the management of renal failure patients. Included in the book are antibacterial drugs, drugs used in the treatment of tuberculosis and fungal infections, drugs used in the treatment of gout, arthritis and inflammatory disorders, anticoagulants, antihypertensive agents, diuretics, antiarrhythmic drugs, immunosuppressive and antineoplastic agents, hypoglycemic drugs, analgesics and soporifics, and drugs used in neurology and psychiatry. A comprehensive drug reference, this book discusses the pharmacology, adverse effects, dialysis properties and appropriate dosage modifications required for renal failure patients. *'76, 246 pp., 1 il., 18 tables, $19.50*

ARTIFICIAL INSEMINATION (2nd Ed.) *by* **Wilfred J. Finegold,** *Univ. of Pittsburgh, Pittsburgh, Pennsylvania. Foreword by* **Alan F. Guttmacher.** This completely revised Second Edition discusses both the pros and cons of artificial insemination, and covers the ethical, religious, legal and psychological ramifications of the procedure. The book also clearly delineates those couples for whom artificial insemination is useless and those for whom it will be advantageous. A history of the test-tube process is included along with a new chapter on insemination with the sperm of the husband. *'76, 156 pp., $12.50*

THE RENAL UPTAKE OF RADIOACTIVE MERCURY ($^{197}\mathrm{HgCl}_2$): Method for Testing the Functional Value of Each Kidney, Technique–Results–and Clinical Application in Urology and Nephrology *edited by* **Claude Raynaud,** *Service Hospitalier Frederic Joliot, Orsay, France. Foreword by* **Pierre Royer.** *(41 Contributors)* Several techniques of uptake measurement are described in the first chapters of this text along with simplified systems of external counting, scanners or gamma cameras, and specific problems associated with the deep position of the kidney or Hg metabolism. The remainder of the book discusses the normal values of Hg renal uptake as well as the results obtained in patients. *'76, 248 pp., 110 il., 47 tables, $22.75*

CLINICAL ASPECTS OF UREMIA AND DIALYSIS *edited by* **Shaul G. Massry** *and* **Alvin L. Sellers,** *both of the Univ. of Southern California School of Medicine, Los Angeles. Foreword by* **George E. Schreiner.** *(40 Contributors)* A totally comprehensive and up-to-date description of the various aspects of the uremic syndrome and its effect on the different organs is presented in this book. Neurological, cardiovascular, hematopoietic, gastrointestinal and metabolic changes are emphasized and a thorough assessment of all the diverse techniques, forms and styles of dialysis as they are practiced today is included. *'76, 768 pp. (6 3/8 x 9 5/8), 264 il., 80 tables, $59.75*

CLINICAL SEROLOGY (7th Ptg.) *by* **Clois W. Bennett.** *Foreword by* **John J. Andujar.** This book details all important serological procedures utilized in the medical diagnostic laboratory including explanation of the particular process and step-by-step procedures for performing the test. Basic principles of immunology and serology, antibodies and their interaction, additional material on types of antigen-antibody reactions, theories of antibody formation, serial dilutions, and others are included. The chapter on syphilis includes information as to types of antibodies, relation of titers in various test procedures and the effect of treatment on the titer. *'75, 304 pp., 15 il., 38 tables, $10.00*

Orders with remittance sent by air, postpaid

301-327 East Lawrence Avenue • Springfield • Illinois • 62717 • USA

In Radiography

Conray Contrast Media

Products of distinction in their substance and shadow

'Conray' contrast media are formulations of either meglumine iothalamate, sodium iothalamate or combinations of the two. These high iodine/low viscosity preparations have an established record of excellence in providing wide margins of safety and tolerance for the patient together with optimum visualization in a comprehensive range of radiographic procedures.

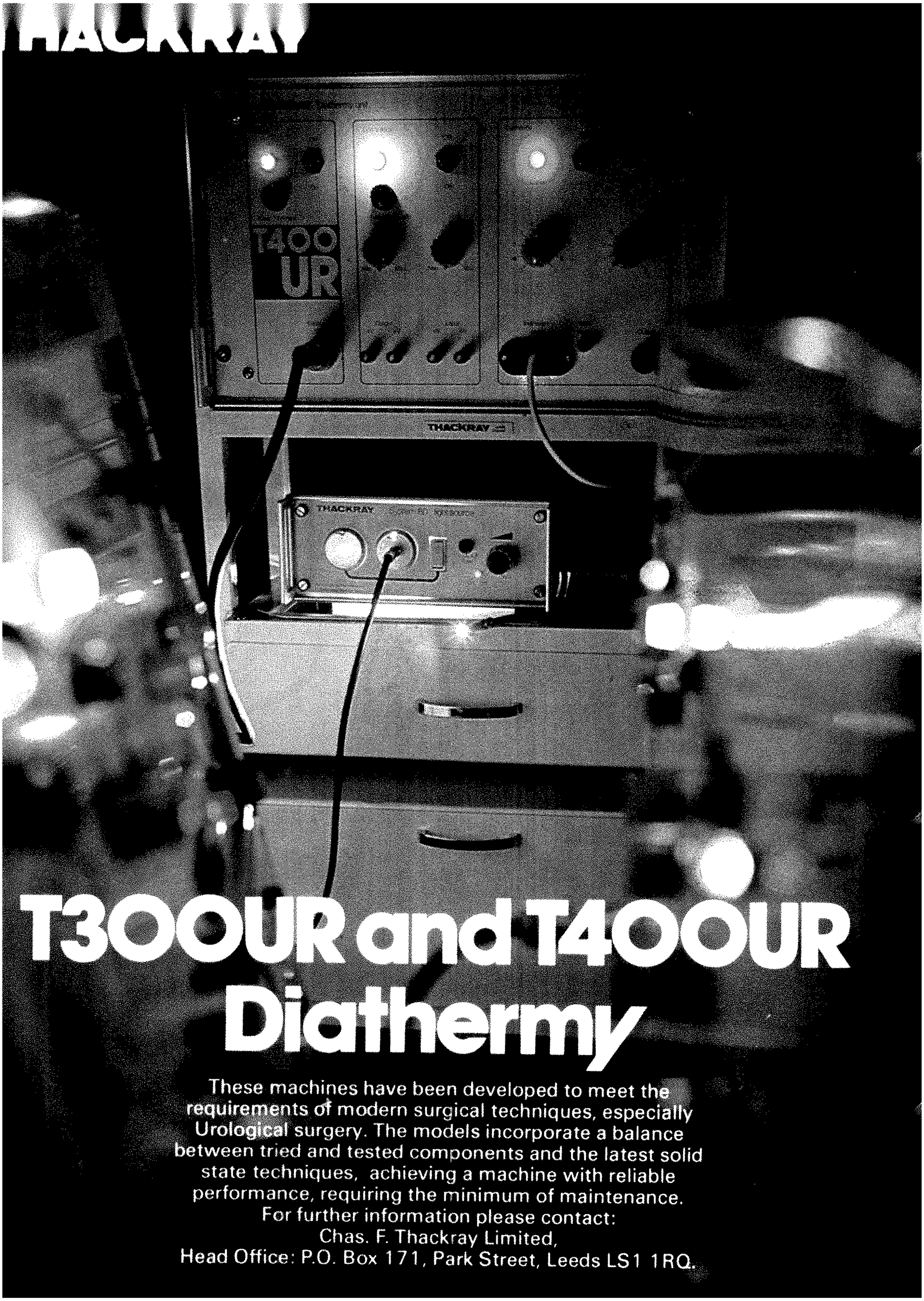
Full information on 'Conray' 280, 'Conray' 325,
'Conray' 420, Cardio-'Conray', Retro-'Conray'
and Gastro-'Conray' supplied on request to
May & Baker Ltd Dagenham Essex RM10 7XS
*trade mark of Mallinckrodt Inc.

Conray*
Contrast Media–
A salt for all reasons
A view of all regions

M&B May & Baker

A member of the Rhône-Poulenc Group of Companies rP

MA 3132



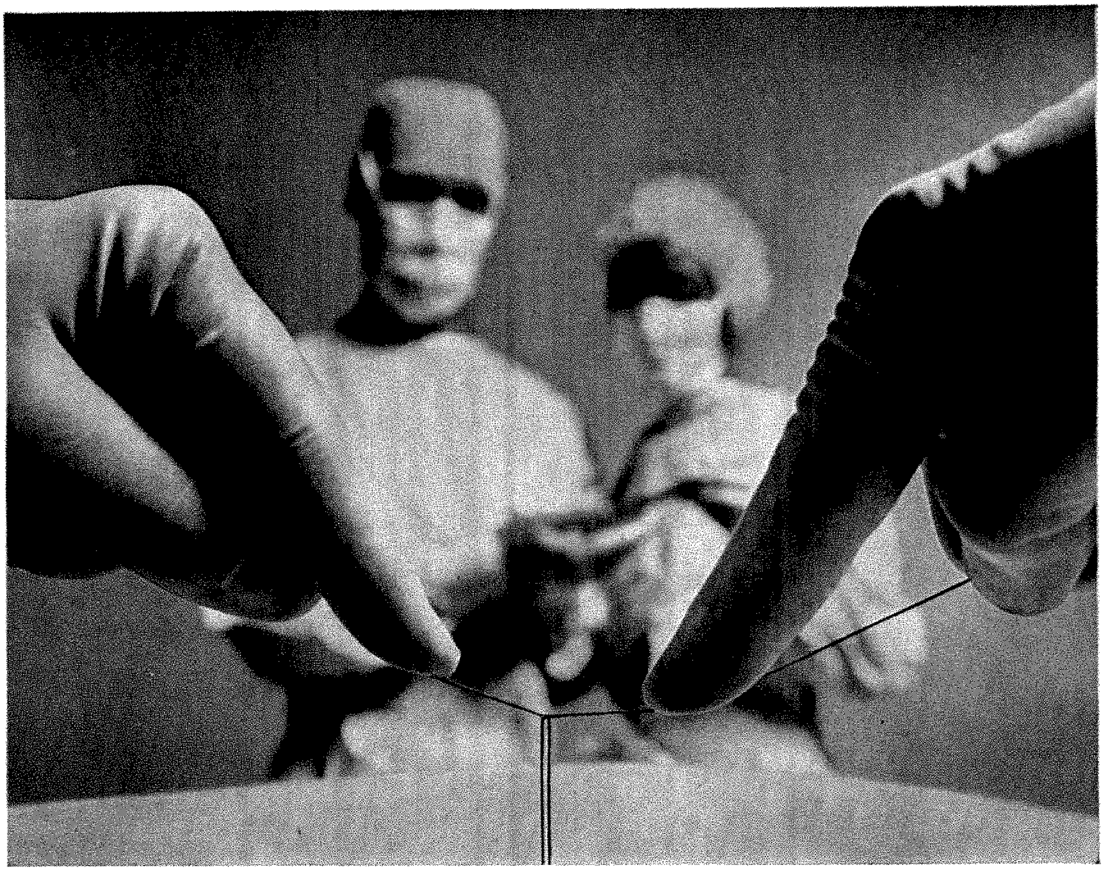
HACKRAY

T300UR and T400UR Diathermy

These machines have been developed to meet the requirements of modern surgical techniques, especially Urological surgery. The models incorporate a balance between tried and tested components and the latest solid state techniques, achieving a machine with reliable performance, requiring the minimum of maintenance.

For further information please contact:
Chas. F. Thackray Limited,
Head Office: P.O. Box 171, Park Street, Leeds LS1 1RQ.

Monofilament. Smooth



Because of the even diameter of ETHICON* Surgical Gut along its entire length, the smooth monofilament surface finish makes passage through tissue easier and smoother and produces less trauma.

Catgut beds down smoothly and securely with even the first throw of the knot and holds securely and strongly with standard surgical knots.

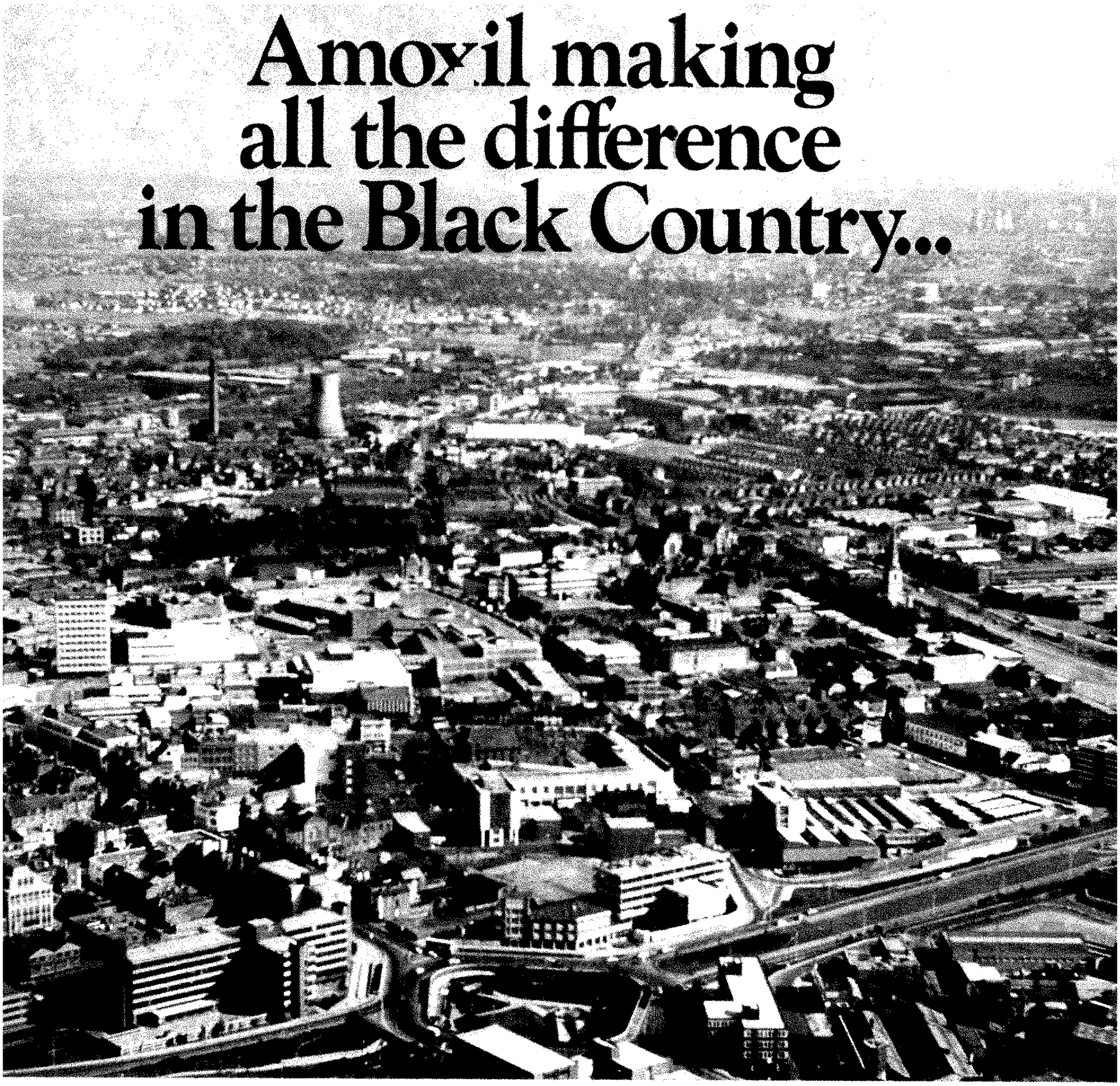
But we're not stopping there. Through research and development we continually strive to offer you, the surgeon, the finest absorbable suture available—but that's only some of the reasons why ETHICON surgical gut is today's most widely used suture material.

Catgut places a world of experience at your fingertips.

When the difference is between being sure and being absolutely certain.

PLR 0508/5002

© ETHICON Ltd 1976 *Trademark



And throughout Britain. Because doctors everywhere now recognise the advantages of Amoxil in respiratory infections.

Amoxil ensures faster relief of symptoms[1] for all respiratory patients and longer periods free from infection for the chronic cases[2].

Three main factors are responsible for this. Firstly, Amoxil is more completely absorbed into serum[3]. Secondly, unlike other antibiotics it penetrates equally well through inflamed and uninflamed bronchial membrane barriers[4] to clear even the most entrenched pockets of infection[5]. And thirdly, extensive studies have shown that Amoxil kills bacteria more rapidly than other antibiotics[6,7].

These three factors, together with a trouble-free dosage, contribute to the Amoxil difference which is appreciated by doctors and patients everywhere.

**makes all the difference
in respiratory infections everywhere.**

ioner (1974), 212, 123.
sherapy (1973), 18, (Suppl.) (19), 1.
d J. (1972), 3, 13.
sta Med. I.C.S. (1974) No. 326, 130
ed. J. (1973), 47, 719.
icrob. Ag. Chem. (1975), 7, (2), 179.
otics under the Microscope: A film
available to the medical profession.

cribing information on Amoxil (regd t.
lin, is available from Bencard.
est Road, Brentford, Middlesex

encard

British Journal of Urology (1976), **48**, 221-226 ©

Surgical Correction of Arterial Stenosis in Renal Allografts

D. E. OSBORN, J. E. CASTRO and R. SHACKMAN

Urological and Transplantation Unit, Royal Postgraduate Medical School, Hammersmith Hospital, London

The present paper records our experience of the surgical correction of renal artery stenosis which occurred in 9/177 patients who were transplanted between 1967 and 1975.

6 of the 9 occurred in females and 3 in males. The mean age of the recipients was 30 years (range 17-38). In 8 patients the kidneys were from cadaver donors and one was from a sibling. In 7/9 the recipients' own kidneys had been removed before or within 5 months of kidney transplantation. In 5 this was for the primary renal disease (pyelonephritis in 3, glomerulonephritis in 2) and in 2 for hypertension. The mean age of the donors was 23 years (range 8-34).

The kidney from the single live donor was transplanted immediately after irrigation with modified Ringer lactate solution. 6 of the 8 cadaver kidneys were stored in ice after irrigation and 2 were perfused on an Ab Gambro machine before transplantation. The total ischaemic time for the 8 cadaver donor kidneys was from 90 to 1547 minutes (Table I). End-to-end anastomosis of the donor renal artery with the recipient's internal iliac artery was performed in every case. 4 weeks post-transplantation the mean creatinine clearance was 44·3 ± 4 ml/min. At that time, 3 of the recipients required mild antihypertensive therapy but all 9 eventually developed severe hypertension which was not controlled despite therapy with methyldopa, diazoxide, propranolol, bethanidine, clonidine and minoxidil in one or more combinations.

Diagnosis

A presumptive diagnosis of renal artery stenosis was made when persistent hypertension was observed and a bruit (usually low pitched) heard over the site of the transplanted kidney (7/9 cases). In 6/9 renal function had deteriorated but in only 1/9 was significant proteinuria present.

The definitive diagnosis was made in all cases by renal angiography using the Seldinger technique (Seldinger, 1953) with local anaesthesia: the catheter was passed through a contralateral or ipsilateral femoral artery in the groin up into the common iliac artery and sometimes to the bifurcation of the aorta. Urografin was injected by pump or manually; anteroposterior and oblique views were then taken (Fig. 2a). In 8/9 cases the radiological appearances suggested that the stenosis was at the site of the arterial anastomosis; in the remaining case it seemed to be more distal but at operation its position was not different from the others. The length of each stenosis, measured directly on the radiograph, ranged from 1 to 10 mm (mean 4·6 mm) and the breadth 15-50% (mean 33%) of the artery distal to the stenosis. In 3 patients a degree of post-stenotic dilatation was seen on the angiograms, but this dilation was not more than 10% of the distal vessel lumen. The median time between transplantation and the demonstration of renal artery stenosis was 22 weeks (range 6-107 weeks) (Table II). Renin estimations were not done.

Surgery

Access was obtained through a long vertical paramedian abdominal incision with the patient in a moderately steep Trendelenburg tilt. Starting the vascular dissection at the common iliac artery is preferable because the stenosis itself is involved by extensive perivascular fibrosis and it is easy to damage the adjacent renal vein.

In 4/9 cases the renal artery distal to the stenosis was long enough for immediate end-to-end vascular reconstruction after excision of the narrowed segment. In one other case the stenosis was incised and a dacron inlay was sutured to the cut edges to enlarge the lumen. A bulldog clamp applied to the proximal arterial segment prevented bleeding but, as a clamp on the distal segment is unnecessary and restricts mobility of the vessel, it was avoided.

Table I

Case No.	Age		Shared HLA antigen	Total ischaemic time (min)	Primary renal disease
	Recipient	Donor			
1	22	14	...	165	Glomerulonephritis
2	24	26	...	240	Glomerulonephritis
3	22	19	3	753	Hypertension
4	26	8	2	722	Pyelonephritis
5	22	11	2	879	Pyelonephritis
6	17	26	3	960	End-stage renal disease
7	33	24	2	1547†	Tuberculosis
8	38	17	2	825†	Pyelonephritis
9	38	34*	1	90	Glomerulonephritis

*Live donor.
†Perfused on Ab Gambro machine.
HLA tissue matching was not available for cases 1 and 2.

Table II

Case No.	Angiographic diagnosis (weeks after transplant)	Stenosis		Intrarenal vessels
		Length (mm)	Breadth % of distal artery	
1	22	1	30	Normal
2	37	3	40	Normal
3	44	2	50	Normal calibre: irregular outline
4	32	10	40	Reduced
5	107	2	30	Normal
6	19	4	15	Normal
7	16	9	30	Normal
8	22	7	5	Normal
9	6	4	60	Normal

Summary of angiographic appearance when transplant renal artery stenosis diagnosed. Length and breadth of each stenosis, as measured directly on the radiograph.

A reversed autogenous saphenous vein bypass graft was used in 4 cases: the proximal end of the vein graft was anastomosed to the side of the renal artery distal to the stenosis and its distal end was joined end to side to the adjacent ipsilateral common iliac artery (Fig. 2b). A bulldog clamp on the internal iliac artery prevented bleeding when the graft was being sutured to the post-stenotic segment: clamps were only applied to the common and external iliac arteries when the bypass graft was sutured to the common iliac artery. The operation was done as a single-stage procedure in 1/4 cases, but in 3/4 a 2-stage procedure at an interval of 7 days was employed (at the first stage the relevant arteries and the renal vein were dissected free and 7 days later the vascular anastomosis was carried out). The 2-stage operation enabled the effects of mobilising the vessels from the dense perivascular tissues to be assessed angiographically but in no case was there improvement. Where possible, we now use a single-stage procedure.

Renal Biopsy

Renal biopsy of the transplanted kidney was carried out in 7/9 cases (1 of these preceded the vascular reconstruction by 2 months). In 2 it revealed histological evidence of vascular rejection and parenchymal rejection in another 2.

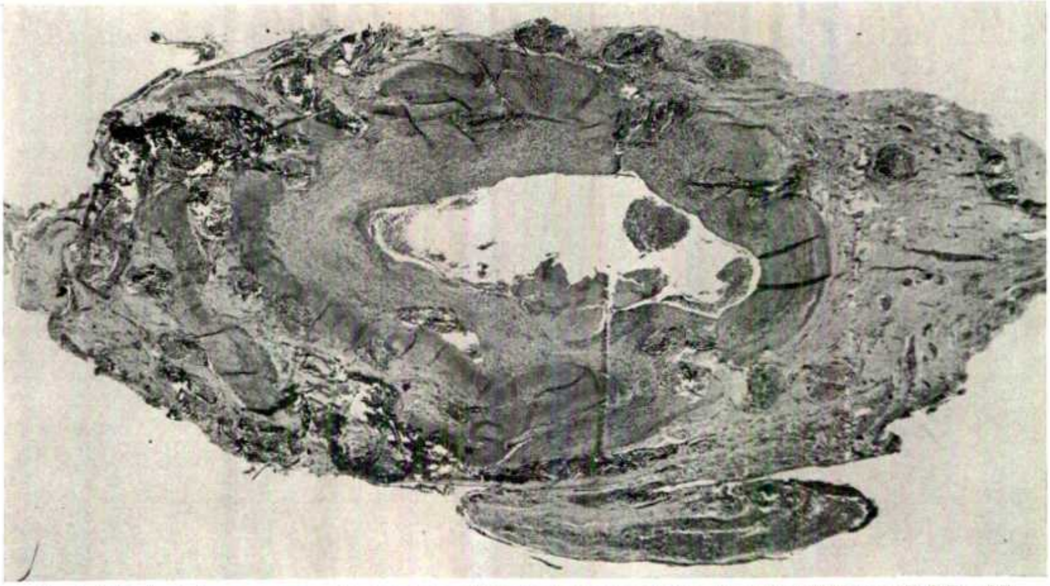


Fig. 1. Histological appearances of a specimen of renal artery stenosis in a transplanted kidney (H & E. × 25).

Histology of Stenosis

Histology of the stenosis was available in 4 cases: there was marked intimal fibrosis at the site of the stenosis in 3 (Fig. 1) and fragmentation of the internal elastic lamina with collagenisation of the media in 1. There was no histological evidence of inflammation.

Subsequent Course

There was no operative mortality, but 2 patients had to be maintained on dialysis and subsequently died as a result of septicaemia within 5 months of operation.

In these 2 patients the renal artery thrombosed soon after the operation and in both cases severe local sepsis followed. 2 others developed anuria immediately after surgical treatment of the stenosis, presumably because of thrombosis of the vascular anastomoses: both are still alive and well, one after a successful live donor kidney transplant and the other on regular dialysis treatment. The operation was successful in the remaining 5 cases: 2 patients are normotensive with good renal function at 2½ and 8 years, 2 are still mildly hypertensive but are controlled with moderate doses of antihypertensive drugs at 12 and 18 months. One remained normotensive for 1½ years until the kidney failed from chronic rejection and she is now on regular dialysis treatment. The results of different forms of surgical treatment are shown in Table III.

Discussion

The cause of renal artery stenosis in a transplanted kidney may vary from one case to another. Sometimes it may be a manifestation of active rejection (Morris *et al.*, 1971) and this appeared to be so in one of our patients. It has been stated that the incidence is greater when cadaver donors are used (Lee, Haregawa and Hume, 1974) and this is supported by our own experience. However, the suggestions that prolonged ischaemia is contributory (Lee *et al.*, 1974) has not been substantiated in our series. Intimal damage, especially during cannulation for irrigation or perfusion, has also been invoked (Smellie, Vinik and Hume, 1969). Certainly, all 9 kidneys referred to in the present report were cannulated and irrigated and 2/9 were continuously perfused for several hours

Table III

Case No.	Treatment	Result
1	Dacron patch	Anuria. Death at 4/12. Septicaemia
2	Excision and end-to-end re-anastomosis	Normotensive at 8 years Serum creatinine 1·2 mg%
3	Excision and end-to-end re-anastomosis	Anuria. Subsequent successful live donor transplant
4	Excision and end-to-end re-anastomosis	Anuria. Maintenance haemodialysis
5	Excision and end-to-end re-anastomosis	Moderate hypertension at 2½ years Serum creatinine 1·1 mg%
6	Saphenous vein bypass graft	Normotensive at 2½ years Serum creatinine 1·1 mg%
7	Saphenous vein bypass graft	Anuria. Death at 5/12. Septicaemia
8	Saphenous vein bypass graft	Chronic rejection of graft. Maintenance haemodialysis after 18 months
9	Saphenous vein bypass graft	Moderate hypertension at 1 year Serum creatinine 1·2 mg%

Summary of surgical treatment and results.

on an Ab Gambro machine. If this factor alone were significant in regard to the development of the stenosis, it is surprising that more cases have not been observed: there was certainly no macroscopic evidence of intimal damage at the time of kidney transplantation in our own cases. Likewise, it is difficult to conclude that the condition was a sequel to the technique employed for the primary arterial anastomosis.

All the patients in this series had end-to-end vascular anastomoses, but in the series reported by Morris *et al.* (1971) renal artery stenosis was as common when the donor renal artery was anastomosed to the side of the common or external iliac artery with a cuff of the donor artery.

A presumptive diagnosis of stenosis may be made with a degree of confidence when a previously fit patient develops hypertension, a bruit is heard over the transplanted kidney, there is no gross increase of proteinuria (Schramek *et al.*, 1975) and antihypertensive drug therapy has to be vigorous and sustained. The main differential diagnosis is rejection and sometimes it is justifiable to prescribe antirejection drugs—even though such treatment may temporarily aggravate the hypertension if it is in fact due to arterial stenosis. Indeed, this was the sequence of events in 5 of our cases. Definitive diagnosis requires angiography: renal biopsy alone may be misleading because rejection and renal artery stenosis may be co-existent and biochemical evidence of deterioration of renal function may occur in both conditions.

Our own practice is to arrange for renal angiography (Raphael *et al.*, 1969) whenever persistent hypertension is observed (with or without an audible bruit), or when antihypertensive drug therapy is either ineffective or intolerable because of its side-effects. Angiography is also undertaken when there are contra-indications to the use of extra doses of antirejection therapy.

It has been stated that renal vein renin may be elevated when there is stenosis in the artery of the transplanted kidney (Bennett *et al.*, 1974), but the values are also increased when there is rejection (Popovtzer *et al.*, 1973) so that it does not help to differentiate between these conditions.

Rarely, the stenosis may undergo spontaneous restitution (Papadimitriou, Chisholm and Shackman, 1969; Schacht *et al.*, 1974) but surgical treatment has to be considered when intensive antihypertensive drug therapy is not effective. Excision of the stenosis and direct re-anastomosis is possible when there is sufficient length of artery: at other times a saphenous vein bypass graft is required.

The results of surgical correction of renal artery stenosis after kidney transplantation are satisfactory in approximately 50% of cases (Lee *et al.*, 1974). In our experience there was complete

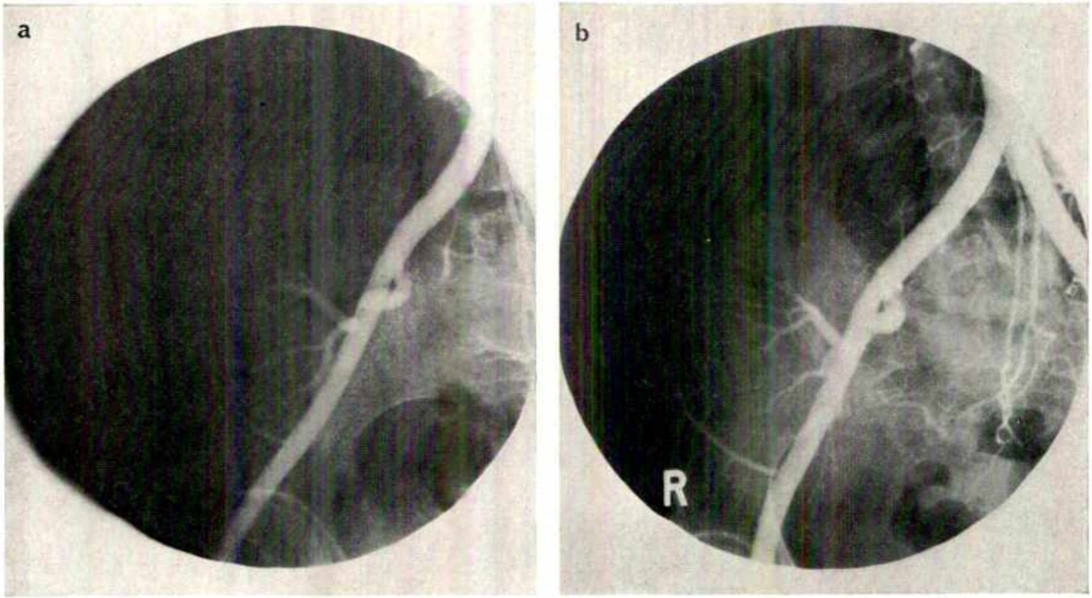


Fig. 2. (a) Renal transplant angiogram demonstrating tight renal artery stenosis at the site of the arterial anastomosis; (b) Angiogram after saphenous vein bypass graft from common iliac artery to renal artery distal to stenosis (case No. 8).

success in 3/9 and partial success in 2/9. The surgery can be difficult and may be followed by arterial thrombosis. There is, therefore, always a chance that the kidney may be "lost" as a direct result of the operative intervention and for this reason surgery should be avoided whenever possible.

Summary

The diagnosis, treatment and results of renal artery stenosis occurring in 9 out of 177 renal transplants are described.

We are most grateful to Professor R. Steiner and his colleagues for the renal angiography, and to Miss J. Paxton and Miss A. Freemantle for secretarial assistance.

References

Bennett, W. M., McDonald, W. J., Lawson, R. K. and Porter, G. A. (1974). Post-transplant hypertension. *Kidney International*, **6**, 99-108.

Lee, H. M., Haregawa, A. and Hume, D. M. (1974). Renal artery stenosis in kidney transplants. 5th International Congress of the Transplantation Society, Israel, p. 186.

Morris, P. J., Yadav, R. V. S., Kincaid-Smith, P., Anderton, J., Hare, W. S. C., Johnson, N., Johnson, W. and Marshall, V. C. (1971). Renal artery stenosis in renal transplantation. *Medical Journal of Australia*, **1**, 1255-1257.

Papadimitriou, M., Chisholm, G. D. and Shackman, R. (1969). Hypertension in patients on regular haemodialysis and after renal allotransplantation. *Lancet*, **1**, 902-904.

Popovtzer, M. M., Pinnggera, W., Katz, F. H., Corman, J. L., Robinette, J., Lanois, B., Halgrimson, C. G. and Starzl, T. E. (1973). Variations in arterial blood pressure after kidney transplantation. *Circulation*, **47**, 1297-1305.

RAPHAEL, M. J., STEINER, R. E., SHACKMAN, R. and WARE, R. G. (1969). Post-operative angiography in renal homotransplantation. *British Journal of Radiology*, **42**, 873-885.

SCHACHT, R. A., KARATULASINGHAM, R., FERRIS, F. Z. and MARTIN, D. G. (1974). Renal artery stenosis following renal transplantation. 5th International Congress of the Transplantation Society, Israel, p. 192.

SCHRAMEK, A., BETTER, O. S., ADLER, O., TUMA, S., HASHMONAI, M., BARZILAI, A. and CHAIMOWITZ, C. (1975). Hypertensive crisis, erythrocytosis, and uraemia due to renal artery stenosis of kidney transplants. *Lancet*, **1**, 70-71.

SELDINGER, S. I. (1953). Catheter replacement of the needle in percutaneous arteriography. *Acta Radiologica*, **39**, 368-376.

SMELLIE, W. A. B., VINIK, M. and HUME, D. M. (1969). Angiographic investigation of hypertension complicating human renal transplantation. *Surgery, Gynecology and Obstetrics*, **128**, 963-968.

The Authors

D. E. Osborn, FRCS, Urological Registrar.
J. E. Castro, PhD, MS, FRCS, Lecturer and Consultant Urologist.
R. Shackman, FRCS, Emeritus Professor of Urology.

British Journal of Urology (1976), **48**, 227-230 ©

Autotransplantation of the Kidney for Fibromuscular Dysplasia of the Renal Arteries

S. G. BALL, G. R. GILES, M. S. F. MCLACHLAN and M. R. LEE

University Departments of Medicine and Radiodiagnosis, The General Infirmary, Leeds and University Department of Surgery, St James's Hospital, Leeds

The role of renovascular surgery in the treatment of hypertension has recently become more clearly defined. This has followed to a large extent the development of new techniques which allow the selection preoperatively of patients whose hypertension can be cured by surgery. Identification of a functionally significant lesion in a renal artery usually leads to its correction by reconstruction of the abnormal vessel or, in the presence of extensive disease, nephrectomy.

We present a patient in whom reversal of hypertension was correctly predicted preoperatively by using renal vein renin ratios. Since extensive bilateral renal arterial disease prevented conventional surgery in this patient, autotransplantation of the right kidney was carried out as an alternative procedure (*Lancet*, 1975).

Case Report

A 30-year-old man was found to be hypertensive at a routine medical examination. His blood pressure on admission was 200/150 mm Hg lying but settled without drug therapy to 170/120 mm Hg after 3 weeks rest. There was narrowing of the retinal vessels but no haemorrhages, no exudates and no papilloedema. Clinical examination was otherwise normal.

His full blood count, renal function, serum potassium, 24-hour urinary aldosterone, 24-hour vanillylmandelic acid excretion and chest X-ray were all normal. Intravenous urography was normal. Bilateral selective renal arteriography revealed irregular narrowing of the right renal artery over a 2 cm length with multiple collateral vessels. This narrowing extended into its major branches (Fig. 1a). The left renal artery showed slight narrowing at the origin of its main branches (Fig. 1b). The appearances strongly suggested bilateral fibromuscular dysplasia.

Samples of blood were obtained by selective catheterisation of each renal vein for the determination of plasma renin activity (PRA) by radioimmunoassay (Ball *et al.*, in preparation). The PRA was 5·1 ng/ml/hour in the right renal vein and 3·3 ng/ml/hour in the left renal vein, a ratio of greater than 1·5 to 1. No difference existed between peripheral vein PRA and left renal vein PRA, indicating suppression of renin secretion from the left kidney.

The angiotensin II antagonist, Saralasin (Eaton Laboratories), was infused intravenously in an attempt to lower systemic arterial pressure. An average fall in systolic blood pressure of 20 mm Hg was achieved with an infusion rate of 16 μg/kg/min but no significant change in diastolic pressure occurred. When the infusion was stopped, systolic and diastolic pressures increased markedly (Fig. 2).

In view of these results, particularly the extent of the arterial disease, it was decided to transplant the right kidney to the left internal iliac artery (autotransplantation). The right kidney was explored through the loin. After ascertaining that sufficient main stem renal artery remained distal to the diseased segment, the kidney was completely removed to a sterile work bench and cooled to 4°C with Perfudex (Pharmacia Ltd.). The renal arterial tree was examined and it was found possible to dilate the segmental arteries of first and second order to a diameter of 2 mm or more. The kidney was preserved on Gambro perfusion using a modified protein fraction and 2 hours later was transplanted into the left iliac fossa by conventional techniques. The operation and the postoperative period were uneventful. Histological examination of the removed segment of the renal artery confirmed the diagnosis of fibromuscular dysplasia.

Blood pressure fell to 120/80 mm Hg immediately following the operation and has remained at this level for 6 months without treatment. Intravenous urography 6 months after surgery showed the transplanted kidney to be excreting contrast medium normally. Its size, shape and calyceal pattern were also normal.

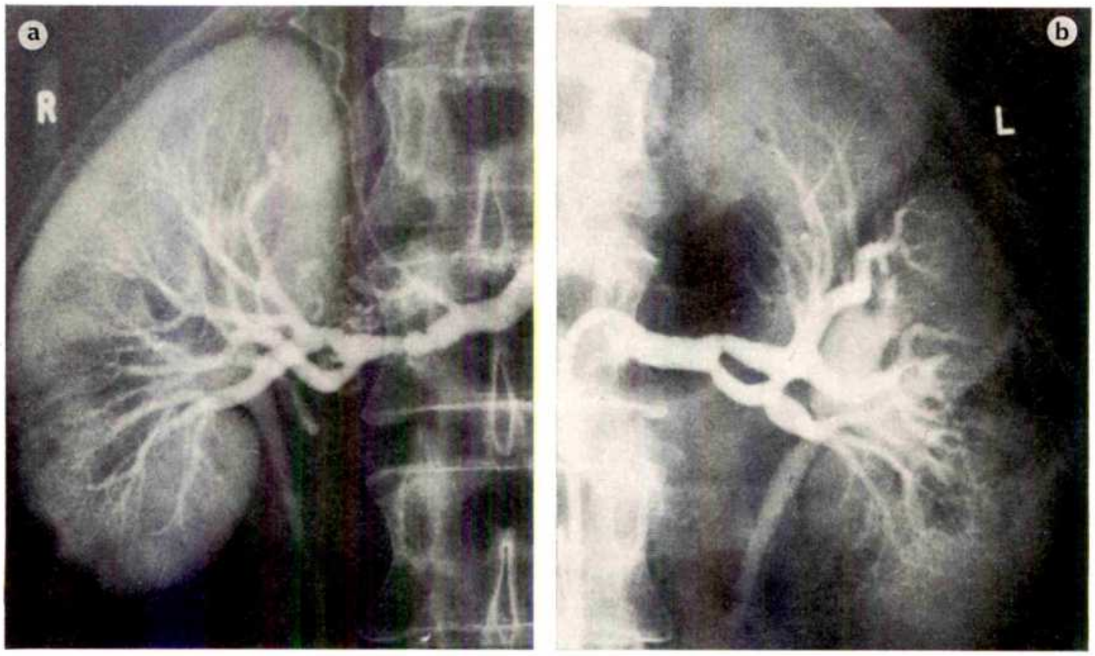


Fig. 1. Selective renal angiography. The distal portion of the right renal artery, (a) shows extensive fibromuscular dysplasia, extending into its major branches. The left renal artery (b) shows narrowing of the origins of its main branches.

Comment

Patients with severe renovascular hypertension may have a normal intravenous urogram in the presence of renal arterial disease, especially if it is bilateral (Lord and Hayes, 1975). Arteriography may show unsuspected stenosis but correction of the vascular lesion will not always lower the blood pressure.

The value of renal vein renin ratios in identifying the kidney responsible for the raised arterial pressure and in predicting the outcome of surgery has become better established in recent years (Vaughan *et al.*, 1973). In our patient the renal vein renin ratio between the right and left kidney was greater than 1·5 to 1, renin secretion by the left kidney being suppressed. It was likely, therefore, that a significant fall in blood pressure would follow surgical correction of the abnormality of the right renal artery.

It has been suggested that a fall in blood pressure in response to the angiotensin II antagonist, Saralasin given intravenously implies a surgically correctable cause for hypertension. This diagnostic test has been used so far in only a small number of patients (Streeten *et al.*, 1975). The fall in systolic pressure of 20 mm Hg in our patient indicates at least a partial response, despite the absence of change in the diastolic pressure. The increase in the blood pressure on stopping the infusion reached a maximum of 40 mm Hg systolic and 30 mm Hg diastolic. This rebound effect may provide additional support for the delineation of a positive response to Saralasin. A low sodium diet or the use of diuretics have been advocated to increase sensitivity to Saralasin in doubtful responders and might have been helpful in this patient.

Finally, even extensive disease can be corrected without loss of functioning renal tissue by using the technique of autotransplantation. Clunie *et al.* (1975) have carried out this operation on 10 patients. 3 had fibromuscular dysplasia of the renal arteries; in 1 patient this was bilateral.

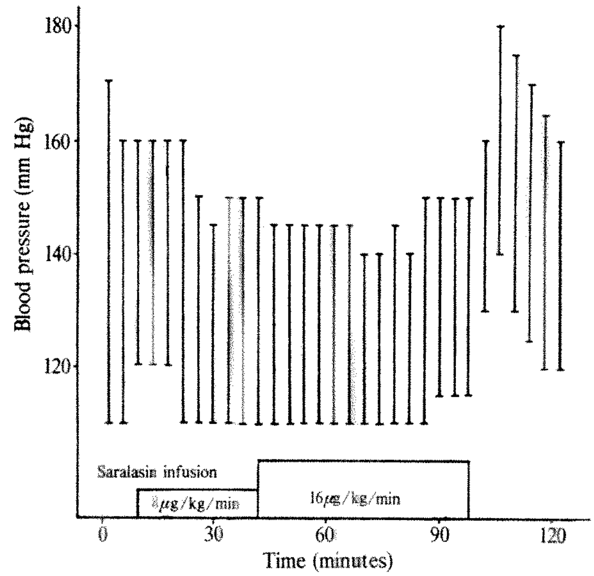


Fig. 2. Response of the blood pressure to the infusion of Saralasin.

Following surgery the blood pressure become normal in 2 of these patients and showed an improvement in the third. The risk of this procedure was no greater than alternative surgical techniques.

The patient we report had disease in both renal arteries. Removal of the right kidney was not indicated and a by-pass operation would have been difficult in view of the extensive nature of the vascular lesions. By autotransplantation it was possible to remove the diseased arterial segment and at the same time to dilate first and second order segmental arteries before reimplantation. This latter technique of graduated dilation, initially used with long-term success in the treatment of fibromuscular disease of the carotid arteries by Morris, Lechter and DeBakey (1968) has since been adapted for treatment of similar disease of the renal arteries (Fry, Brink and Thompson, 1970; Ernst *et al.*, 1972). In view of the bilateral renal arterial disease, we are unable to predict the future course of this patient's blood pressure, but in the short term we have achieved a significant reduction. Autotransplantation of the kidney has corrected a lesion which was probably inoperable by conventional methods.

Summary

A young man was discovered to have symptomless hypertension, which subsequently proved to be caused by fibromuscular dysplasia of the renal arteries.

Arterial disease was present on both sides but was more severe on the right. Samples of blood were obtained by selective catheterisation of each renal vein for the determination of plasma renin activity. The renal venous renin was greater on the right than on the left (ratio greater than 1·5 to 1) and secretion of renin by the left kidney was suppressed.

Autotransplantation of the right kidney to the left internal iliac artery lowered the blood pressure at once and it has remained normal for 6 months.

The implications of this procedure for the management of a bilateral disorder of the renal arteries, such as fibromuscular dysplasia, are discussed.

S. G. Ball is supported by the Medical Research Council.

M. R. Lee thanks the Wellcome Trust for financial support.

The patient was initially referred by Dr P. Newcombe from York City Hospital, to Professor G. P. McNicol, Department of Medicine, Leeds General Infirmary.

We also thank Mrs N. Elliot for her skilled technical assistance and Dr P. Heyburn for liaising between hospitals.

We also thank Mrs M. Vero and Eaton Laboratories for making Saralasin acetate available to us.

References

BALL, S. G., ELLIOT, N. L. and LEE, M. R., (in preparation).

CLUNIE, G. J. A., GORDON, R. D., HARTLEY, L. C. J., PETRIE, J. J. B. and HARDIE, I. R. (1975). Results of surgical treatment of renovascular hypertension. *Medical Journal of Australia*, **1**, 225-228.

ERNST, C. B., STANLEY, J. C., MARSHALL, F. F. and FRY, W. J. (1972). Autogenous saphenous vein aortorenal grafts. *Archives of Surgery*, **105**, 855-862.

FRY, W. J., BRINK, B. E. and THOMPSON, N. W. (1970). New techniques in the treatment of extensive fibromuscular disease involving the renal arteries. *Surgery*, **68**, 959-967.

Lancet (1975). Editorial, **1**, 961.

LORD, R. S. A. and HAYES, J. M. (1975). Renovascular reconstruction in hypertension. *Medical Journal of Australia*, **1**, 240-246.

MORRIS, G. C., LECHTER, A. and DEBAKEY, M. E. (1968). Surgical treatment of fibromuscular disease of the carotid arteries. *Archives of Surgery*, **96**, 636-643.

STREETEN, D. H. P., ANDERSON, G. H., FREIBERG, J. M. and DALAKOS, T. G. (1975). Use of an angiotensin II antagonist (Saralasin) in the recognition of "angiotensinogenic" hypertension. *New England Journal of Medicine*, **292**, 657-696.

VAUGHAN, E. D., BÜHLER, F. R., LARAGH, J. H., SEALEY, J. E., BAER, L. and BARD, R. H. (1973). Renovascular hypertension: renin measurements to indicate hypersecretion and contralateral suppression, estimate renal plasma flow and score for surgical curability, *American Journal of Medicine*, **55**, 402-414.

The Authors

S. G. Ball, MRCP, M.R.C. Research Fellow, Department of Medicine.

G. R. Giles, MD, FRCS, Professor of Surgery.

M. S. F. McLachlan, MD, FRCPE, FRCR, Professor of Radiodiagnosis.

M. R. Lee, DM, DPhil, MRCP, Consultant Senior Lecturer in Clinical Pharmacology, Department of Medicine.

British Journal of Urology (1976), **48**, 231-233 ©

Vaginal Ureterolithotomy

P. J. O'BOYLE and N. O. K. GIBBON
Regional Urological Centre, Sefton General Hospital, Liverpool

The surgical management of the low ureteric calculus has been revolutionised by the development of endoscopic techniques of extraction (Constantian, 1974). Nevertheless, not infrequently in urological practice is it necessary to remove an impacted calculus which has failed to respond to conventional manoeuvres. The abdominal approaches, whether retroperitoneal, transperitoneal or transvesical, each have their advocates but also their difficulties, particularly in the obese patient or following previous pelvic surgery. It is our contention that the simplest surgical approach in the female is through the lateral vaginal wall. This provides rapid and easy access to the lower ureter. We have used this method on 5 occasions in the last 2 years and in 2 cases have been thwarted by proximal displacement of the stone which was subsequently removed by open operation.

The fundamental indication for the vaginal approach is the removal of a low ureteric calculus which can be readily palpated through an adequate vagina and which is not amenable to endoscopic extraction. It may also be used to advantage in the poor risk or toxic patient.

Technique

With suitable vaginal retraction the cervix is grasped and displaced to the opposite side. The calculus is gently palpated and an incision made through the overlying vaginal mucosa and the tough supporting fascia. Careful blunt dissection with the finger and if necessary a curved artery forceps readily reveals the ureter. The uterine artery can be palpated anteriorly. The ureter is gently mobilised above the calculus and a fine rubber catheter passed encircling the ureter and trapping the stone to prevent upward displacement. A longitudinal incision directly over the calculus allows delivery and subsequently a catheter is passed via the ureterostomy to ensure there is no distal obstruction which would require dilatation. The ureter is reconstituted with 4/0 chromic catgut and the vaginal wall loosely closed. No drainage is necessary.

Case 1

S. A., an extremely obese 35-year-old para 1, was an emergency admission due to right lower ureteric obstruction with infection and a fulminating pyrexia. Her previous history included hyperparathyroidism and three abdominal operations, *viz.* cholecystectomy, appendicectomy and excision of uterine fibroids. Pyelography revealed a poorly functioning right kidney with a large calculus obstructing the lower ureter. A retrograde catheter would not pass beyond this.

On vaginal examination the calculus was easily palpable and ideally suited the vaginal approach. Through a lateral vaginal incision the ureter was mobilised and a fine rubber catheter passed to control the ureter and trap the calculus. The ureter was incised and the calculus delivered without difficulty. Ureteric catheterisation showed no evidence of distal obstruction so the ureteric walls were apposed with two 4/0 chromic catgut sutures.

Postoperatively there was minimal leakage per vaginam for 7 days. This stopped spontaneously. Since that time she has remained well.

Case 2

M. G., a 45-year-old para 4+1, had a 5-year history of recurrent right iliac fossa pain. Routine investigation revealed a large calculus in the right lower ureter with upper tract dilatation.

Vaginal ureterolithotomy allowed easy delivery of the calculus. There was no subsequent urinary leakage and she was discharged on the 4th postoperative day. She remains well with normal renal function.

Case 3

H. K., a 36-year-old woman with a 3-year history of recurrent left pyelonephritis had multiple renal and ureteric calculi, gross hydronephrosis and non-function of the left kidney. A left nephrectomy and partial ureterectomy were performed but subsequently she was troubled by deep pelvic pain and developed a sinus from the stump of the left ureter. Radiography showed that the remaining ureter was filled with pultaceous material and small calculi which could not be removed satisfactorily with the Dormia extractor. In view of the persistent sinus and infection an abdominal approach would have been extremely difficult. Through a left lateral vaginal incision the ureter was opened and all residual calculi and associated material removed. Postoperatively she made an uneventful recovery and remains completely well.

Case 4

C. E., a 54-year-old woman, presented with right ureteric colic and was found to have an impacted stone in the lower ureter which could not be removed endoscopically. Since this was readily palpable per vaginam vaginal ureterolithotomy was attempted. Following the mucosal incision the calculus escaped proximally and required open ureterolithotomy.

Case 5

M. W., a 71-year-old woman with widespread pyramidal lesions following a cervical spine injury, was admitted to the Spinal Injury Unit for removal of egg shell calculi from the bladder and of a large calculus producing obstruction in the left lower ureter. Endoscopy revealed widespread cystitis and multiple calculi which were crushed and extracted. The ureteric calculus was readily palpable but following vaginal incision promptly disappeared. 4 weeks later the cystitis had cleared and the ureteric calculus was removed with the Dormia extractor following incision of the ureteric orifice.

Discussion

Vaginal ureterolithotomy is a safe and easy method of removing stones from the lower ureter yet has received scant mention in the current textbooks and recent urological literature. As Dodson, Sipe and Lord (1957) have indicated, the method was described in 1879 by Emmet in his book *Principles and Practice of Gynaecology*. Garvey and Gomberg (1946) in a review article discuss the main advantages of the technique and its complications and dispel the notion that vesico-vaginal fistula is a common complication. They argue that fistula formation is an ever present hazard also with the abdominal approach and certainly the subsequent surgical management is no more difficult. Another prevalent fear is of damage to the uterine artery and certainly the prospect of haemorrhage from this source is somewhat daunting. However, when we consider the facility with which our gynaecological colleagues perform their manoeuvres in this region and the remarkably low morbidity perhaps this too is exaggerated. Provided the anatomical relationships are borne in mind and care is taken in the blunt dissection this complication should be avoided. Likewise bleeding from the vaginal wall can usually be readily controlled. The main problem which we have encountered has been due to proximal displacement of the calculus during mobilisation of the ureter. This might be prevented by engaging the calculus with a loop or basket prior to the dissection in some instances.

Finally, if this method is unsuccessful for any reason it will be necessary to resort to an abdominal approach but we feel that little will have been lost in the attempt and certainly the results in our experience have been most gratifying.

Summary

The vaginal approach to the low ureteric calculus may provide an easy, rapid and safe solution to a difficult surgical problem. It is important to select the case with care and, provided basic surgical principles are followed, the complications should be minimal.

3 recent successful cases are described and a further 2 in which the technique failed due to proximal displacement of the stone. The importance of adequately immobilising the calculus prior to ureterotomy is emphasised.

References

CONSTANTIAN, H. M. (1974). Management of ureteral calculi: series of 574 cases with special emphasis on use of Davis loop extractor. *Journal of Urology*, **112**, 33-35.
DODSON, A. I. (1970). Surgery of the ureter. In, *Urological Surgery*, A. I. Dodson (Editor). Saint Louis: Mosby, 251-253.
DODSON, A. I., SIPE, W. R. and LORD, K. H. (1957). The treatment of patients with ureteral calculi. *Journal of Urology*, **78**, 575-584.
GARVEY, F. K. and GOMBERG, D. (1946). Vaginal ureterolithotomy. *Journal of Urology*, **56**, 49-56.

The Authors

P. J. O'Boyle, FRCS, Senior Surgical Registrar.
N. O. K. Gibbon, FRCS, Consultant Urologist.

British Journal of Urology (1976), **48**, 234 ©

Short Case Report

Appendix Ureteroplasty

The use of the appendix in urology as a tube to replace a segment of ureter has been reported by Melnikoff (1912) and Wesolowski (1971). This paper reports its use in a further case.

Case Report

A Rhodesian African male, aged 18 years, presented with a 6-week history of a constant left loin pain associated with a swelling in this area. Micturition was normal. *S. Haematobium* infestation had been treated 7 years previously.

Examination revealed an enormous cystic mass in the left loin. Blood pressure 160/130.

Blood urea 90 mg. Electrolytes normal. Haemoglobin 12·1 g. Viable *S. Haematobium* ova in the urine.

IVP (90-min film) showed no function on the left with a marked hydronephrosis on the right side. Cystoscopy revealed a gross diffuse chronic schistosomal picture with the left ureteric orifice strictured completely and the right ureteric orifice admitting a 3F catheter for 2 cm only, making retrograde pyelography impossible. The diagnosis at this stage was bilateral ureteric strictures due to schistosomiasis and exploration advised after conservative therapy reduced his urea to 43 mg.

Operation. A lower abdominal "suitcase" type of incision was used (Fig. 1). The left functionless hydronephrosis was removed, together with the strictured ureter to the bladder. Then right lower ureterectomy was carried out to include 2·5 cm of normal ureter above the stricture. The appendix was then isolated and anastomosed to normal ureter and to the bladder. Splinting with a Gibbon's catheter was used with Foley urethral bladder drainage. Postoperative recovery was complicated by a urinary leak at bladder level but with 8 weeks urethral drainage, healing took place. At this stage, blood urea was 23 mg and the 90-min IVP film showed a decrease in the size of the hydronephrosis.

Comment

The lower abdominal "suitcase" type incision has been found very useful for our cases where extensive exploration of both the ureters is needed in bilateral schistosomal stricturing of the ureters. In this case, the appendix was seen to be anatomically suitable in position, length (15 cm) and mesentery vascularity to restore urinary continuity. Anastomoses were carefully carried out because our experience has shown in bilharzial cases that this is necessary as they have a tendency not to heal. Despite this, a leak in fact did occur.

There is little doubt that ileal loop replacement is the method of choice in extensive ureterectomy for schistomosomal strictures Weinberg (1970). However, as Hovnanian (1972) has suggested, the odd case may arise where the use of the appendix may prove to be suitable because of its anatomical arrangement as in the present case.

We thank the Secretary for Health for permission to publish this case.

R. W. Weinberg—, Part-time lecturer.
Department of Urology, Godfrey Huggins School of Medicine, Salisbury, Rhodesia

References

Hovnanian, A. P. (1972). Ureteral replacements. *Surgery, Gynaecology and Obstetrics*, **135**, 810-818.

Melnikoff, A. E. (1912). Sur le remplacement de l'uretère par une anse isolée de l'intestin grêle. *Revue Clinique d'Urologie*, **1**, 601-603.

Weinberg, R. W. (1970). Extensive schistosomiasis of the ureter—the use of the ileal loop in its management. *British Journal of Urology*, **42**, 136-139.

Wesolowski, S. (1971). Corrective operative procedure after unsuccessful pelvi-ureteric plastic surgery. *British Journal of Urology*, **43**, 679-686.

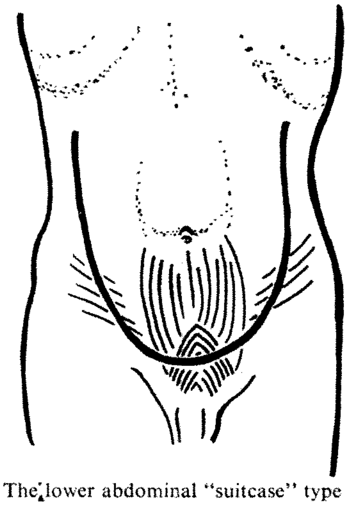


Fig. 1. The lower abdominal "suitcase" type incision.

British Journal of Urology (1976), **48**, 235-238 ©

Preliminary Communication

The Use of Bromocriptine in the Treatment of the Unstable Bladder

D. J. FARRAR and J. L. OSBORNE
Urodynamic Clinic, Middlesex Hospital, London

The management of the unstable bladder poses a difficult problem. Patients present with a diversity of symptoms from disturbing frequency, nocturia and urgency to socially unacceptable incontinence. These symptoms result from uninhibited bladder contractions which the patient is unable to control and may even be unaware that they are occurring. Detrusor instability itself may occur as a consequence of overt neurological disease, or in the male, as a result of outflow tract obstruction (Turner-Warwick *et al.*, 1973). However, the majority of patients belong to a primary (idiopathic) group in which the aetiology is unknown.

A variety of operations to denervate the bladder have been designed in an attempt to control these uninhibited detrusor contractions but the results are disappointing. Recently, however, some success has been reported in the treatment of detrusor instability both by Torrens and Griffith (1974) using a more selective denervation technique and by Dunn, Smith and Ardran (1974) using prolonged bladder distension; but both of these are invasive techniques.

Drugs remain the first line of treatment for primary detrusor instability. The commonly used drugs aim at modifying detrusor activity either by direct anticholinergic activity or by the stimulation of β adrenergic receptors. Although Moolgaoker *et al.* (1972) have reported good results from drug treatment, other workers have achieved only limited success, often with a high incidence of unacceptable side-effects in the therapeutic dose range (Brown, Arnold and Worth, 1973; Stanton, 1973) and this has also been our experience.

Following a recent trial of bromocriptine (2 bromo-α-ergocriptine: C.B.154. Sandoz) in males with benign prostatic hypertrophy it was suggested that this drug might also have a place in the treatment of the unstable bladder (Farrar and Pryor, 1976). This paper reports our preliminary experience with the use of bromocriptine in the treatment of patients with detrusor instability.

Patients and Methods

7 male patients (aged 29 to 72 years) and 17 female patients (aged 17 to 69 years) form the basis of this report. All 24 patients had presented with persistent and troublesome micturition symptoms and were known to have detrusor instability diagnosed by the technique of videocystography with synchronous pressure/flow studies (Bates, Whiteside and Turner-Warwick, 1970; Bates, 1971; Bates and Corney, 1971; Arnold, 1974).

The essential features of this technique consist of measuring the detrusor pressure by electronic subtraction of the abdominal (rectal) pressure from the total bladder pressure. The bladder is filled with the patient in the supine position at about 100 cc/min with contrast medium (35% Diodone), whilst a continuous filling cystometrogram is obtained. Bladder filling proceeds until the patient has a strong desire to micturate. The patient is then tilted erect. If the cystometry up to this point is equivocal then the Diodone is emptied back into the container and another filling cystometrogram is obtained in the erect posture. The patient is also asked to cough several times as unstable detrusor contractions may be provoked by coughing.

In a normal case the detrusor muscle is unaffected by the provocative tests of rapid filling both erect and supine, assuming the erect posture and vigorous coughing with a full bladder. A rise in detrusor pressure of up to 10 cm

H_2O during any one of these provocative tests can be accepted as within normal limits (Arnold, 1974). Detrusor instability is diagnosed if there is a sustained rise of detrusor pressure above these limits.

5 of the male patients had long-standing detrusor instability in spite of effective relief of their outlet obstruction; the remaining 2 male patients and all the 17 female patients had primary (idiopathic) detrusor instability not associated with either obstruction or overt neuropathy. 21 of the patients had previously received treatment with either drugs or vesical distension or both without success.

Our initial experience with bromocriptine in patients with detrusor instability showed that there was considerable variation in the tolerated dose and it was therefore necessary to decide initially the optimum dosage for each individual patient. All patients therefore commenced treatment with capsules containing 1 mg of bromocriptine, although it was not often possible to exceed a dose of 5 mg a day in divided doses because of the development of side-effects. Not all patients benefited symptomatically from bromocriptine; however, its effectiveness in those who did was further tested by a double blind trial. The patients who entered the double blind trial either continued on bromocriptine or received identical capsules containing an inert powder (placebo); allocation to these groups was random and depended upon a code held by the hospital pharmacy.

A detailed micturition history was obtained from all patients before commencing treatment, particular attention being paid to the frequency of diurnal and nocturnal voiding and to the presence or absence of urgency of micturition; where incontinence was present, an attempt was made to differentiate urge from stress incontinence. Response to treatment was assessed symptomatically, although patients were accepted as being improved only if there was objective evidence of reduction in the frequency of diurnal or nocturnal voiding.

The double blind trial lasted for 6 weeks as it was not thought justified to continue placebo treatment for longer. The patients were asked to monitor their progress by completing a weekly questionnaire of their micturition symptoms; and these symptoms were reviewed again at the end of the trial.

Results

10 of the 24 patients who commenced treatment failed to obtain any symptomatic relief from bromocriptine and 5 of these patients also had marked side-effects including headache, nausea, lethargy and constipation.

The remaining 14 patients (3 males and 11 females) all appeared to benefit symptomatically from bromocriptine: 11 of these patients having previously been treated with either drugs or vesical distension without improvement.

4 of the 14 patients subsequently did not complete the trial; 1 patient stopped his treatment in the middle of the trial because of marked symptomatic improvement that had occurred and he felt that further treatment was not required; 1 patient contracted infectious mononucleosis whilst on the trial and treatment was therefore discontinued; 2 patients discontinued treatment because of side-effects of nausea, lethargy and constipation.

10 patients completed the double blind trial. 6 continued in the double blind part of the trial on bromocriptine and in all but 1 the symptomatic improvement was maintained. 4 patients received the placebo as part of the double blind trial and in 3 of these patients there was a relapse of symptoms, which improved again on returning to a known dose of bromocriptine at the end of the trial.

An analysis of the improvement in micturition symptoms of the 14 patients who responded to treatment is shown (Table)

Side-effects in these patients who responded to treatment, apart from the patients already discussed, were minimal; consisting of mild constipation in 5 and postural giddiness initially in 3.

Table

Micturition symptoms of patients who responded to treatment with Bromocriptine

Symptoms	No. of patients	Patients improved on bromocriptine	Patients not improved on bromocriptine
Frequency	14	14	0
Nocturia	14	14	0
Urgency	14	10	4
Urge incontinence	9	7	2
Stress incontinence	8	4	4

2 female patients who responded symptomatically to bromocriptine agreed to another videocystogram. Both patients still had unstable bladders on cystometry; in 1, however, the functional bladder capacity was doubled and in the other there was a marked reduction in voiding detrusor pressure (without development of residual urine).

This change in cystometry, especially associated with a change in symptoms would suggest that there had been some modification of detrusor activity by the drug.

2 patients have now been receiving bromocriptine for at least 6 months with continuing amelioration of symptoms.

Discussion

In evaluating the results of treatment of the unstable bladder the varied aetiology of this condition should be considered. Even within the primary (idiopathic) group it is probable that there are a number of different aetiological factors; it is therefore, not surprising that there is no completely effective single treatment for this condition.

Our results show that over half of the 24 patients with detrusor instability responded symptomatically to treatment with bromocriptine. The symptoms of persistent frequency, nocturia and urgency with or without urge incontinence are commonly associated with detrusor instability and all 14 patients who responded to treatment noticed an improvement in their symptoms. On the other hand, in those patients who in addition complained of stress incontinence the improvement of this symptom which on the whole is a result of sphincter weakness, was not marked. Overall those patients who responded to treatment felt that the quality of their life had been improved by amelioration of their micturition symptoms.

The effectiveness of bromocriptine in the treatment of detrusor instability has been confirmed by the double blind trial. Whilst the number of patients studied is too small for statistical analysis, the relapse of symptoms which occurred with the placebo and subsequent improvement on returning to bromocriptine was most striking.

It is of interest that bromocriptine was less well tolerated on a patient/dose basis in our series than in patients described by other workers in other spheres (Varga *et al.*, 1972; Calne *et al.*, 1974; Thorner *et al.*, 1975); it is possible that our patients with detrusor instability form a particularly sensitive group in their responses to this drug.

The mode of action of bromocriptine upon the unstable bladder is unknown. It is known to have properties as a dopamine receptor stimulator (Corrodi *et al.*, 1973). Thorner (1975) has recently reviewed the role of dopamine in the peripheral nervous system and has shown its wide distribution; it would seem possible that bromocriptine, acting as a dopamine agonist, might cause a reduction in detrusor muscle activity either by modulating cholinergic transmission or by acting directly, although the site of this action is unknown, and remains open to speculation. Further work is required to evaluate the mode of action of this drug in patients with primary detrusor instability, work which may give some guide to at least one aetiology of this condition.

Summary

Initial experience with the use of bromocriptine in 24 patients with troublesome micturition symptoms associated with an unstable bladder is described.

14 patients responded symptomatically to treatment with bromocriptine and these results were confirmed by a double blind trial in this group.

11 of these patients had previously failed to benefit from treatment either with drugs or vesical distension.

It is concluded that bromocriptine has a part to play in the treatment of some cases of primary detrusor instability.

We would like to acknowledge the help and advice given by the late Dr E. R. Evans of Sandoz, who also provided the capsules for this trial.

References

Arnold, E. P. (1974). Cystometry: postural effects in incontinent women. *Urologia Internationalis*, **29**, 185-186.

Bates, C. P. (1971). Continence and incontinence. *Annals of the Royal College of Surgeons*, **49**, 18-35.

Bates, C. P. and Corney, C. E. (1971). Synchronous cine pressure flow cystography: a method of routine urodynamic investigation. *British Journal of Radiology*, **44**, 44-50.

Bates, C. P., Whiteside, C. G. and Turner-Warwick, R. T. (1970). Synchronous cine pressure flow cystourethrography with special reference to stress and urge incontinence. *British Journal of Urology*, **42**, 714-723.

Brown, A. D. G., Arnold, E. P. and Worth, P. H. L. (1973). The unstable bladder: a study of drug treatment in women. Paper read at the 3rd International Continence Society Meeting, Copenhagen.

Calne, D. B., Leigh, P. N., Teychenne, P. F., Bamji, A. N. and Greenacre, J. K. (1974). Treatment of Parkinsonism with bromocriptine. *Lancet*, **2**, 1355-1356.

Corrodi, H., Fuxe, K., Hökfelt, T., Lidbrink, P. and Ungerstedt, U. (1973). Effect of ergot drugs on central cathecholamine neurons. *Journal of Pharmacy and Pharmacology*, **25**, 409-411.

Dunn, M., Smith, J. C. and Ardran, G. M. (1974). Prolonged bladder distension as a treatment of urgency and urge incontinence of urine. *British Journal of Urology*, **46**, 645-652.

Farrar, D. J. and Pryor, J. S. (1976). The effect of bromocriptine in patients with benign prostatic hypertrophy. *British Journal of Urology*, **48**, 73-75.

Moolgaoker, A. S., Ardran, G. M., Smith, J. C. and Stallworthy, J. A. (1972). The diagnosis and management of urinary incontinence in the female. *Journal of Obstetrics and Gynaecology of the British Commonwealth*, **79**, 481-497.

Stanton, S. L. (1973). A comparison of emepronium bromide and flavoxate hydrochloride in the treatment of urinary incontinence. *Journal of Urology*, **110**, 529-532.

Thorner, M. O. (1975). Dopamine is an important neurotransmitter in the autonomic nervous system. *Lancet*, **1**, 662-664.

Thorner, M. O., Chait, A., Aitken, M., Benker, G., Bloom, S. R., Mortimer, C. H., Sanders, P., Stuart Mason, A. and Besser, G. M. (1975). Bromocriptine treatment of acromegaly. *British Medical Journal*, **1**, 299-303.

Torrens, M. J. and Griffith, H. B. (1974). The control of the uninhibited bladder by selective sacral neurectomy. *British Journal of Urology*, **46**, 639-644.

Turner-Warwick, R. T., Whiteside, C. G., Worth, P. H. L., Milroy, E. J. G. and Bates, C. P. (1973). A urodynamic view of the clinical problems associated with bladder neck dysfunction and its treatment by endoscopic incision and transtrigonal posterior prostatectomy. *British Journal of Urology*, **45**, 44-59.

Varga, L., Lutterbeck, P. M., Pryor, J. S., Wenner, R. and Erb, H. (1972). Suppression of puerperal lactation with an ergot alkaloid: a double blind study. *British Medical Journal*, **2**, 743-744.

The Authors

D. J. Farrar, FRCS, Clinical Research Fellow (now Department of Urology, Manchester Royal Infirmary).
J. L. Osborne, MRCOG, Clinical Research Fellow.

British Journal of Urology (1976), **48**, 239-243 ©

Bladder and Urethral Innervation in Multiple Sclerosis

JENS T. ANDERSEN and WILLIAM E. BRADLEY

Department of Neurology, University of Minnesota, Minneapolis, Minnesota

Studies of neurogenic dysfunction of the bladder and urethra in multiple sclerosis have mainly been based on cystometry and sphincter electromyography (Bradley, Logothetis and Timm, 1973). In recent years the technique of signal tracing in the nervous system has been applied to the delineation of impairment of the innervation of the detrusor muscle and urethra (Bradley, 1972). 52 patients with multiple sclerosis were studied utilising this new technique. The study showed impairment of the segmental innervation of the bladder and urethra in the majority of the patients with definite signs of impaired volitional control of the function of the pudendal motor nucleus. Thus evidence of demyelinating plaques in the lumbosacral cord was detected with the technique.

Patients and Methods

38 female and 14 male patients were studied. The mean age of the patients was 41·9 years (range 22 to 73 years) and the mean duration of multiple sclerosis was 12·2 years (range 1 to 36 years). The symptomatology, the cystometric and sphincter electromyographic findings in these patients, have been reported in a previous paper (Andersen and Bradley, 1976).

A contractile response was evoked in the anal sphincter and periurethral striated muscle by electrical stimulation of the proximal urethra and the intrinsic bladder wall. This reflex (Fig. 1) consists of an afferent sensory pathway from the urethra and detrusor to the sacral grey matter, where the afferent impulses are interrupted in synapses on the pudendal motor neurons. Excitation of the pudendal motor neurons triggers action potentials in the pudendal motor nerve eliciting a contractile response in the periurethral striated muscle, anal sphincter and the pelvic floor musculature (Fig. 2).

We used a specially designed indwelling urethral catheter with externally mounted concentric stimulating electrodes. After insertion of the catheter into the bladder the balloon was inflated and the catheter snugged against

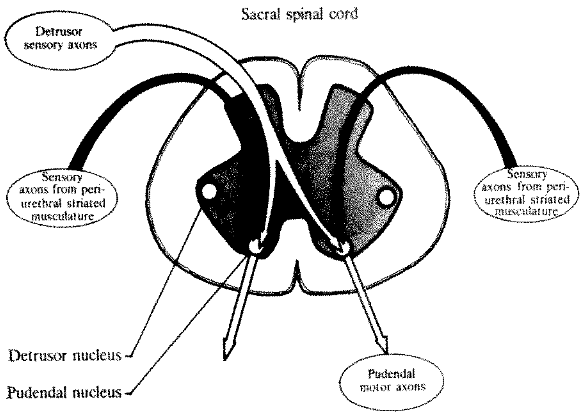

Sacral spinal cord
Detrusor sensory axons
Sensory axons from peri-urethral striated musculature
Sensory axons from peri-urethral striated musculature
Detrusor nucleus
Pudendal nucleus
Pudendal motor axons

Fig. 1. Schematic drawing of the neural circuit governing the spinal evoked responses. Stimulation of the sensory axons from the detrusor and periurethral striated musculature trigger action potentials in the pudendal motor nerve.

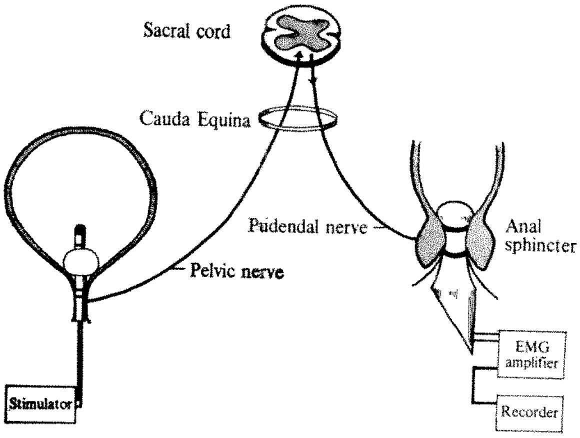


Fig. 2. Illustration of the set-up for recording of spinal evoked responses.

③

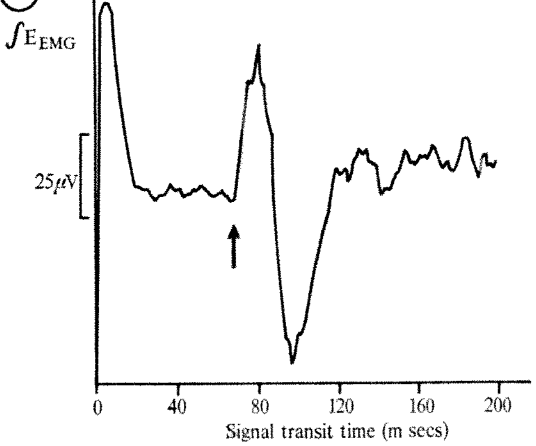


Fig. 3. Response evoked in anal sphincter by stimulation of the proximal urethra.

the bladder neck to ensure that the distal electrodes were in contact with the mucosa of the proximal urethra. An electrical stimulator connected to the electrodes provided pulses ranging in amplitude from 4 to 40 volts with a pulse duration of 0·1 to 0·2 msec.

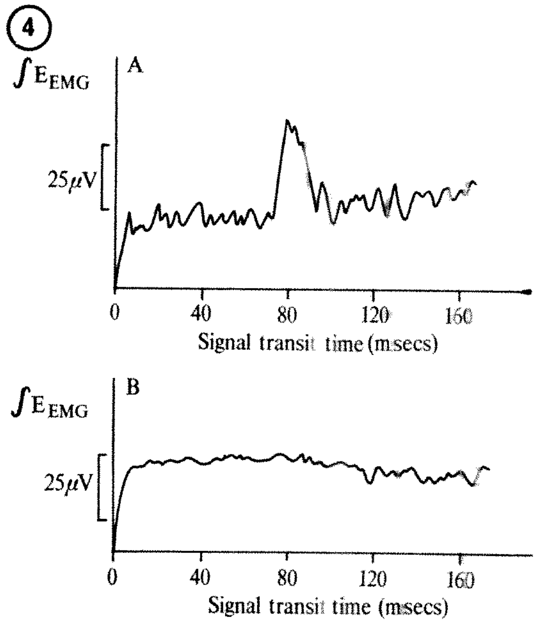
Anal sphincter activity was recorded utilising an hour-glass-shaped Teflon anal plug with externally mounted concentrical recording electrodes. 16 to 64 EMG-responses were integrated and cyclically averaged by a digital signal averager and recorded on a strip chart recorder. The response evoked by stimulation of the bladder wall was obtained by applying a slight vacuum on the urethral catheter in order to affix the bladder wall to the proximal recording electrode on the catheter, and the stimulation-recording procedure was repeated. The amplitude of the evoked responses varied from 25 to 150 microvolts. From the recordings the latency or signal transit time through the reflex arc was registered (Fig. 3).

The integrity of the voluntary, supraspinal control of the pudendal nucleus was tested by asking the patients to relax the perineum. In patients with intactness of the corticospinal tract this procedure abolished the evoked responses (Fig 4), whereas in patients with lesions of the pyramidal tract the evoked response could not be voluntarily suppressed (Fig. 5).

Results

Spinal-evoked Responses

The distribution of the evoked anal sphincter EMG responses evoked by stimulation of the proximal urethra is shown in Figure 6. The latencies in healthy volunteers have been reported



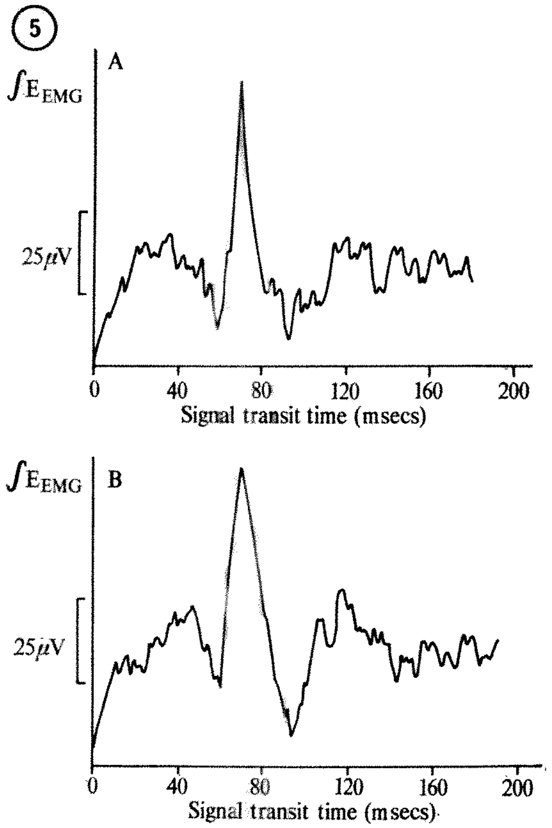
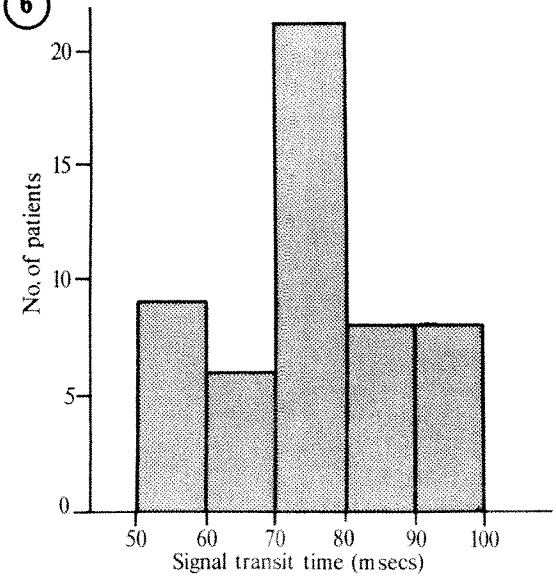


Fig. 4. (*a*) Response evoked in anal sphincter by stimulation of proximal urethra in a 50-year-old male with a 6-year history of multiple sclerosis, (b) Suppression of the response after the patient was instructed to relax the perineum.

Fig. 5. Impairment of the supraspinal innervation of the pudendal nucleus in a 24-year-old female with a 7-year history of multiple sclerosis. (a) Anal evoked response. (b) Loss of ability to suppress the evoked response by instructing the patient to relax the perineum.

ranging from 50 to 70 msec (Bradley, 1972). In this study only 15 patients had latencies within this normal range, whereas the remaining 37 patients showed prolonged latencies. This is presumably due to partial impairment of the involved reflex arc because of demyelinating plaques localised in the lumbosacral portion of the spinal cord. The voluntary suppression of the evoked response was tested in 32 of the patients. 29 patients were not able to inhibit the response on command, and these patients all showed bilateral extensor plantar responses documenting impairment of the corticospinal tract. 3 patients were able to suppress the evoked response on command and they all had normal plantar reflexes.

Stimulation of the bladder wall evoked responses in the anal sphincter in 50 of the patients. In 2 patients no response could be elicited in the anal sphincter by stimulation of the bladder wall indicating a block in the reflex arc. These 2 patients both had detrusor areflexia on the cystometric recordings. The distribution of the latencies is shown in Figure 7. 50% of the patients showed signal transit times longer than 70 msec. The mean latency of the responses evoked by stimulation of the bladder wall was 70·7 msec, whereas the mean latency by stimulation of the proximal urethra was 78·5 msec. This difference is not statistically significant.



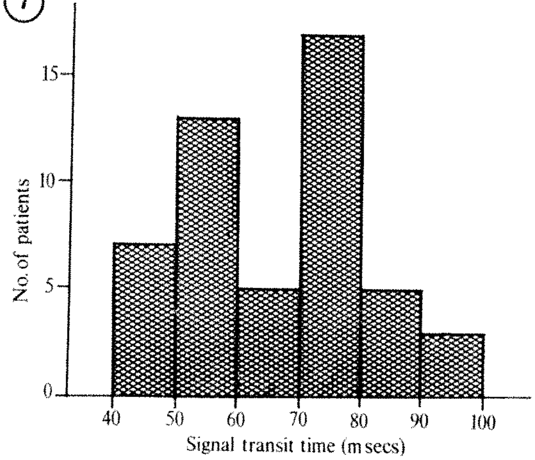


Fig. 6. Distribution of the signal transit times of responses evoked in the anal sphincter by stimulation of the proximal urethra.

Fig. 7. Distribution of the signal transit times of responses evoked in the anal sphincter by stimulation of the bladder wall.

Discussion

Evoked reflex latency measurement has been a useful technique in the present study in the delineation of the innervation of the bladder and urethra. The findings of prolonged signal transit times in the majority of the patients is extremely valuable for the understanding of the pathophysiology of the disturbances of bladder and urethral innervation which can be documented by cystometry and sphincter EMG (Andersen *et al.*, 1975).

Prolonged signal transit times were found as well in the patients with presence of the detrusor reflex as in the patients with detrusor areflexia. Detrusor abnormalities were present in all the patients who were unable to inhibit the evoked response. No correlation was found between the disturbances of sphincter control and the lack of ability voluntarily to suppress the evoked response. The documented impairment of the corticospinal innervation of the pudendal nucleus confirms the pathoanatomical studies by Fog (1950) showing that the demyelinating plaques of the spinal cord in multiple sclerosis were mainly localised to the corticospinal and reticulospinal tracts.

Summary

Bladder and urethral innervation was studied in 52 patients with multiple sclerosis using a signal tracing technique (evoked reflex latency measurement).

The majority of the patients showed prolonged signal transit times indicative of demyelinating plaques localised to the lumbosacral spinal cord. Furthermore, impairment of the corticospinal innervation of the pudendal nucleus was found in 29 patients indicating lesions of the pyramidal tract.

This work was supported in part by a research grant from the National Institute of General Medical Sciences number GM-21178.

References

ANDERSEN, J. T., and BRADLEY, W. E. (1976). Abnormalities of detrusor and sphincter function in multiple sclerosis. *British Journal of Urology*, **48**, 193-198.

BRADLEY, W. E., LOGOTHETIS, J. L. and TIMM, G. W. (1973). Cystometric and sphincter abnormalities in multiple sclerosis. *Neurology*, **23**, 1131-1139.

BRADLEY, W. E. (1972). Urethral electromyelography. *Journal of Urology*, **108**, 563-564.

FOG, T. (1950). Topographic distribution of plaques in the spinal cord in multiple sclerosis. *Archives of Neurology and Psychiatry*, **63**, 382-414.

The Authors

Jens T. Andersen, MD, Assistant Professor.
William E. Bradley, MD, Professor.

British Journal of Urology (1976), **48**, 244 ©

Short Case Report

Ectopia Vesicae Complicated by Squamous Cell Carcinoma

Carcinomatous changes in ectopia vesicae occur at an early age and in 95% instances it is adenocarcinoma. Epidermoid carcinoma of exstrophied bladder is extremely rare. It is usually of low-grade malignancy and it seldom, if ever, metastasises (Riches, 1951).

Case History

A 48-year-old male was admitted on 13 September 1973 with dribbling of urine since birth and a fleshy growth in the suprapubic region of 6 months duration. Almost the entire mucosa of his exstrophied bladder was covered with exuberant growth which bled on touching (Fig. 1).

An IVP showed good excretion from both kidneys.

At operation there was no evidence of tumour-spread beyond the bladder wall and the general peritoneal cavity and liver were free from metastases. Both ureters were implanted separately into the sigmoid colon. The bladder with its tumour, together with the cut lower ends of the ureters, were excised. The cavity in the abdominal wall was closed after immobilisation of the rectus muscle, rectus sheath and the overlying skin.

He made an uneventful postoperative recovery and is alive and well to date.

Histopathological examination of the excised specimen revealed that the bladder mucosa was replaced by a malignant infiltrating squamous epithelium with large numbers of epithelial pearl formation and keratinisation (Fig. 2). The malignant cells showed pleomorphism and even giant cell formation. There was an associated ulceration and heavy infiltration of interstitial tissue with lymphocytes and plasma cells. The tumour was richly vascular.

Comment

The overall incidence of carcinoma of exstrophied bladders has been given as 4% (7 in 170) at the Mayo Clinic (Goyanna, Emmett and McDonald, 1951) and 7·5% (3 in 42) at Johns Hopkins Hospital (Engel and Wilkinson 1970). O'Kane and Megaw (1968) could collect only 55 cases of exstrophied bladders from the literature and added 1 case of their own. Out of these 56 cases only 2 were squamous cell carcinoma.

S. Gupta and I. M. Gupta
Department of Surgery and Pathology, Institute of Medical Sciences, Banares Hindu University, India

References

Engel, R. M. and Wilkinson, H. A. (1970). Bladder exstrophy. *Journal of Urology*, **104**, 699-704.

Goyanna, R., Emmett, J. L. and McDonald, J. R. (1951). Exstrophy of the bladder complicated by adenocarcinoma. *Journal of Urology*, **65**, 391-400.

O'Kane, H. O. J. and Megaw, J. M. (1968). Carcinoma in the exstrophic bladder. *British Journal of Surgery*, **55**, 631-635.

Riches, E. W. (1951). Ectopia vesicae. *Annals of the Royal College of Surgeons*, **9**, 71-79.

Reprint requests to: Dr. S. Gupta, 2-medical Enclave, B.H.U. Campus, Varanasi-221005, India.

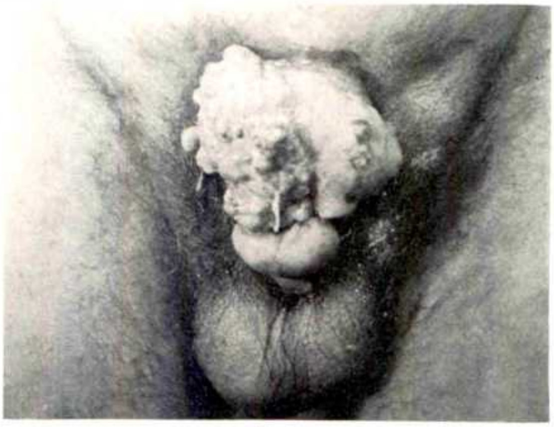


Fig. 1

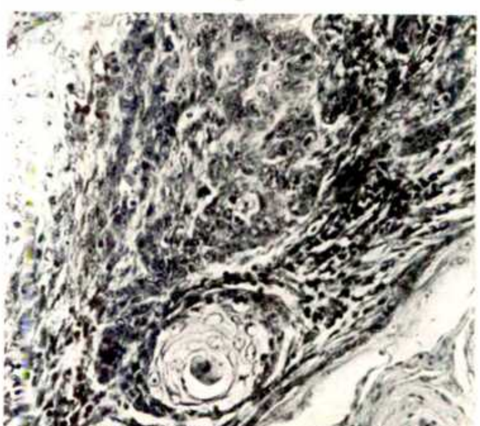


Fig. 2

British Journal of Urology (1976), **48**, 245-253 ©

Chronic Bacterial Prostatitis: New Therapeutic Aspects

A. PFAU and T. SACKS

Departments of Urology and Clinical Microbiology, Hadassah University Hospital, Jerusalem, Israel

In 1968, Meares and Stamey stated that, in the absence of any other pathology, chronic persistence of Gram-negative entero-bacteria in the prostate is the commonest cause of relapsing urinary tract infections in males. In the same year, Winningham, Nemoy and Stamey (1968) showed that most of the antibacterial drugs, which are effective in urinary tract infections, are ineffective in curing infections of the prostate gland because of the difficulty with which they cross the epithelial membrane of this gland. The same study suggested that an effective antibacterial drug, able to cross the barrier of the prostatic epithelial membrane and reach therapeutic concentrations in the prostate, should be a lipid soluble base with a high pKa and active against Gram-negative bacteria at the prostatic pH. Trimethoprim was presented as such a drug, effective in chronic bacterial prostatitis (Reeves and Ghilchik, 1970; Carroll *et al.*, 1971).

Only a few well-documented cases of chronic bacterial prostatitis have been published to date (Meares and Stamey, 1968; Stamey, 1972; Meares, 1973; Meares, 1975). The purpose of this paper is to describe our experience with this entity and to discuss its clinical and therapeutic aspects.

Patients and Methods

6 male patients with recurrent urinary tract infections, in whom no other gross pathological findings could be detected on physical or laboratory examinations, were incorporated in this study.

The technique used for localising lower urinary tract infections in the male has been described (Stamey, Govan and Palmer, 1965; Meares and Stamey, 1968). This method is based upon quantitative bacterial counts of 3 separate voided urine specimens. The third voided urine specimen, collected after prostatic massage, which was used at the beginning of this study, was later replaced by a specimen of pure prostatic secretion, collected immediately after the patient had completely emptied his bladder. The patients were advised to abstain from sexual intercourse for at least 5 days before the examination. All the specimens were collected by the senior author (A. P.) personally. After collection, the samples were immediately transferred to the laboratory, refrigerated at 4°C and cultured within 2 hours.

Quantitative cultures were performed by surface colony counts on blood agar plates (Difco blood agar base with 5% human blood). Colony counts were performed after 24 hours' incubation at 37°C. Bacterial identification was by standard methods. Sensitivity testing was by disc diffusion technique.

Case Reports

Case 1. E. P., a 54-year-old male, had his first episode of chills, fever up to 39°C, right flank tenderness, dysuria and frequency in October 1971. The urine culture at that time yielded *E. coli*. His symptoms cleared after treatment with ampicillin and chloramphenicol.

When first seen by us on 15 November, 1971, the patient had only slight dysuria. Physical examination revealed a slightly enlarged, smooth and non-tender prostate. The urine culture on admission grew 100,000 *E. coli* per ml. The IVP was normal. The patient was given nitrofurantoin for the next 10 days and the urine became sterile. During the following year his symptoms recurred 4 times after medication was stopped. The urine cultures yielded

Table I

Bacteriologic History of E. P., a 54-year-old male

Date	Days on (+) or off (−) drug	Drug	Colonies/ml*				Organism
			1	2	EPS	3	
Oct 18, 1972	−178	Cotrim.	6,000	20,000	...	400	*E. coli*
Oct 22, 1972	+1	Nitrofur.	0	0	0	...	...
Oct 24, 1972	+3	Nitrofur.	0	0	0	...	...
Oct 30, 1972	+9	Nitrofur.	50	0	70	...	*E. coli*
Oct 31, 1972	+10	Nitrofur.	80	0	500	...	*E. coli*
Nov 6, 1972	−6	Nitrofur.	800	0	...	1,000	*E. coli*
Nov 19, 1972	−19	Nitrofur.	200	0	5,000	...	*E. coli*
Nov 26, 1972	−26	Nitrofur.	0	0	2,000	...	*E. coli*
Dec 6, 1972	−36	Nitrofur.	8,000	120	100,000	...	*E. coli*
Dec 10, 1972	−40	Nitrofur.	100,000	100,000	7,000	...	*E. coli*
Dec 17, 1972	+6	Cotrim.	0	0	0	...	...
Apr 1, 1973	+110	Cotrim.	0	0	0	...	...
May 28, 1973	−44	Cotrim.	0	0	0	...	...
July 7, 1975	−27m	Cotrim.	0	0	0	...	...

Abbreviations used in the table are as follows: 1 = first voided 5 to 10 ml of urine (urethral); 2 = midstream urine specimen (bladder); EPS = expressed prostatic secretion; 3 = first voided 5 to 10 ml of urine after prostatic massage (prostatic). Nitrofur. = nitrofurantoin; Cotrim. = cotrimoxazole; m = months.

* Low counts of Gram-positive organisms (staphylococci, streptococci, diphtheroids) were not included in the Table.

Table II

Bacteriologic History of U. Z., a 66-year-old male

Date	Days on (+) or off (−) drug	Drug	Colonies/ml*				Organism
			1	2	EPS	3	
Oct 4, 1972	−3	Ampi.	0	0	400	...	*P. mir.*
Oct 9, 1972	−8	Ampi.	35,000	100,000	8,000	...	*P. mir.*
Oct 16, 1972	+6	Cotrim.	0	0	0	...	...
July 4, 1975	−854	Cotrim.	0	0	0	...	...

Abbreviations used in the table are as follows: 1 = first voided 5 to 10 ml of urine (urethral); 2 = midstream urine specimen (bladder); EPS = expressed prostatic secretion; 3 = first voided 5 to 10 ml of urine after prostatic massage (prostatic). Ampi. = ampicillin; Cotrim. = cotrimoxazole.

* Low counts of Gram-positive organisms (staphylococci, streptococci, diphtheroids) were not included in the Table.

E. coli, with the same sensitivity pattern on each occasion. The treatment used during this period was nitrofurantoin, nalidixic acid, sulphamethizole and cotrimoxazole, each for 10 days.

In view of the recurrent urinary tract infections despite usually effective antibacterial treatment, differential urine cultures were performed. These remained sterile for the next 6 months, at which time the patient again developed urinary discomfort. All 3 urine cultures grew *E. coli*. Nitrofurantoin was started, and a continuous, almost daily collection of divided urine and prostatic secretion specimens was started on 22 October, 1972 (Table I). These localisation studies suggested that the source of infection was in the prostate. A 4-month treatment with cotrimoxazole was started on 11 December, 1972. Cultures of all the urine samples rapidly became sterile and remained so during the treatment. On 14 April, 1973 the treatment was stopped; repeated urine cultures were sterile and the patient has now remained asymptomatic for 27 months.

Table III

Bacteriologic History of M. K., a 31-year-old male

Date	Days on (+) or off (−) drug	Drug	Colonies/ml* 1	2	EPS	3	Organism
Apr 3, 1975	...	...	350	0	2,800	...	*Pseud.*
Apr 6, 1975	...	...	80	0	1,200	...	*Pseud.*
Apr 12, 1975	+5	Cotrim.	800	0	3,500	...	*Pseud.*
Sep 7, 1975	−2	Cotrim.	0	0	0	...	...
Sep 19, 1975	−14	Cotrim.	0	0	0	...	...

Abbreviations used in the table are as follows: 1 = first voided 5 to 10 ml of urine (urethral); 2 = midstream urine specimen (bladder); EPS = expressed prostatic secretion; 3 = first voided 5 to 10 ml of urine after prostatic massage (prostatic). Cotrim. = cotrimoxazole.

* Low counts of Gram-positive organisms (staphylococci, streptococci, diphtheroids) were not included in the Table.

Case 2. U. Z., a 66-year-old male, was referred on 5 March, 1972 because of frequency and dysuria for the preceding year. Physical examination revealed a slightly enlarged prostate and the IVP a small quantity of residual urine. During the next 6 months (March 1972-September 1972) the patient had 4 relapses of symptomatic *P. mirabilis* urinary tract infections in spite of the fact that treatment with cotrimoxazole or ampicillin resulted in sterilisation of the urine each time. Localisation studies done on 4 October, 1972 (Table II) suggested the prostate as the source of the recurrent *P. mirabilis* infections. 5 days later the patient relapsed with a bladder infection and a 4-month treatment with cotrimoxazole was started. All the cultures became sterile and have remained so for the next 2½ years.

Case 3. M. K., a 31-year-old male, was referred to us because of recurrent urinary tract infections for the past 10 years. Physical examination revealed a left atrophic testicle and a normal prostate. The IVP was negative.

In view of the longstanding history of recurrent urinary tract infections, in the presence of a normal IVP, localisation studies were performed repeatedly. They suggested that the prostate was the source of a *Pseudomonas* infection (Table III). Cotrimoxazole treatment was instituted on 8 April, 1975 and continued for 5 months at which time all the cultures were sterile. Unfortunately, the patient did not return for follow-up in spite of repeated requests.

Case 4. A. Y., a 52-year-old male, was first seen in our hospital on 8 May, 1972 after a recent urinary tract infection. He had felt well until 3 weeks previously when he started to experience suprapubic tenderness, slight difficulty in micturition, dysuria and tenderness in the right testicle. He had received nitrofurantoin and his symptoms had consequently receded.

Physical examination revealed a slightly thickened and tender right epididymis, but was otherwise non-contributory. The IVP was normal.

During the next 6 months (May 1972-October 1972) the patient experienced 3 symptomatic *E. coli* urinary infections which were adequately treated with nitrofurantoin, cotrimoxazole and cotrimoxazole for 30 days respectively.

Localisation studies, started after the last cotrimoxazole treatment, suggested on 2 occasions (22 October, 1972 and 25 October, 1972) that the prostate was the source of the *E. coli* (Table IV). On 3 November, 1972, while not on therapy, the patient had a new bladder infection and this time long-term cotrimoxazole therapy was initiated and continued for 8 months. During the first 4 months of this treatment the cultures of the prostatic secretion repeatedly grew *E. coli* but they all became sterile during the last 4 months of the treatment.

After 8 months of cotrimoxazole therapy, the drug was stopped on 16 July, 1973 (Table IV). This time the segmented urine and prostatic secretion cultures remained sterile for about 7 months, when on 4 February, 1974 the prostatic secretion culture again grew a small number of *E. coli*. 3 weeks later all 3 cultures were infected with *E. coli*. Kanamycin was given i.m. for 14 days without any undesirable effects. The segmented urine and prostatic secretion cultures rapidly became sterile and remained so for the next 19 months, during which time the patient has remained asymptomatic.

Case 5. D. S., a 31-year-old patient, was referred to our hospital on 2 November, 1971 because of a 4-month story of frequency and marked dysuria. Physical examination, IVP and cysto-panendoscopy were repeatedly negative. Between November 1971 and May 1973 the patient experienced 2 urinary infections with *E. coli* and 1 with *Streptococcus faecalis*. Antibacterial therapy (cotrimoxazole, nalidixic acid and ampicillin) achieved sterilisation of the

Table IV

Bacteriologic History of A. Y., a 52-year-old male

Date	Days on (+) or off (−) drug	Drug	Colonies/ml*				Organism
			1	2	EPS	3	
Oct 22, 1972	−4	Cotrim.	0	0	...	70	*E. coli*
Oct 25, 1972	−7	Cotrim.	0	0	...	450	*E. coli*
Nov 3, 1972	−15	Cotrim.	100,000	80,000	100,000	...	*E. coli*
Nov 5, 1972	+2	Cotrim.	0	0	0	...	...
Nov 12, 1972	+9	Cotrim.	0	0	500	...	*E. coli*
Nov 19, 1972	+16	Cotrim.	0	0	0	...	...
Dec 11, 1972	+38	Cotrim.	0	0	1,200	...	*E. coli*
Mar 12, 1973	+128	Cotrim.	0	0	800	...	*E. coli*
May 9, 1973	+184	Cotrim.	0	0	0	...	...
July 11, 1973	+247	Cotrim.	0	0	0	...	...
July 25, 1973	−9	Cotrim.	0	0	0	...	...
Aug 26, 1973	−41	Cotrim.	0	0	0	...	...
Nov 27, 1973	−134	Cotrim.	0	0	0	...	...
Feb 4, 1974	−203	Cotrim.	0	0	30	...	*E. coli*
Feb 27, 1974	−226	Cotrim.	100	4,500	5,000	...	*E. coli*
Mar 21, 1974	+14	Kana.	0	0	0	...	...
Apr 1, 1974	−8	Kana.	0	0	0	...	...
Oct 12, 1975	−568	Kana.	0	0	0	...	...

Abbreviations used in the table are as follows: 1 = first voided 5 to 10 ml of urine (urethral); 2 = midstream urine specimen (bladder); EPS = expressed prostatic secretion; 3 = first voided 5 to 10 ml of urine after prostatic massage (prostatic). Cotrim. = cotrimoxazole; Kana. = kanamycin.

* Low counts of Gram-positive organisms (staphylococci, streptococci, diphtheroids) were not included in the Table.

urine each time. On 2 occasions between June and November 1973 (Table V) localisation studies revealed the prostate as the source of the *E. coli* infections. After treatment with nitrofurantoin the *E. coli* was replaced by a *Proteus mirabilis*. Further localisation studies again showed the prostate as the source of infection and long-term cotrimoxazole therapy was instituted on 16 December, 1973 (Table V). This therapy was not able to eradicate the chronic *P. mirabilis* infection in the prostate and eventually a bladder infection occurred on its 38th day (23 January, 1974). Cotrimoxazole was stopped and kanamycin was given for the next 10 days. The prostatic cultures became rapidly sterile and have remained so for the next 20 months.

Case 6. S. Y., a 56-year-old male, was referred to our hospital on 3 April, 1972 shortly after an attack of frequency, dysuria, low back pain, pains along the lower extremities accompanied by high fever and chills. After treatment with ampicillin the symptoms receded and the urine became sterile. During the next 3 months (April-June 1972) the patient experienced 3 additional similar attacks of *E. coli* urinary tract infection which were successfully treated each time with ampicillin or nitrofurantoin. Localisation studies started in our department (Table VI) showed clearly that the source of the recurrent *E. coli* urinary infections was in the prostate. 2 long-term cotrimoxazole courses (July 1972-October 1972 and November 1972-April 1973) were not able to eradicate the chronic prostatic infection and therefore short-term streptomycin therapy was instituted. The prostatic fluid became sterile. 3 months later localisation studies showed small numbers of *Proteus mirabilis* in the urethral and prostatic specimens but the numbers of bacteria were always greater in the urethral specimen, sometimes the same bacteria grew only in the urethral specimen and often enough all the cultures were sterile. No further treatment was given and the patient has remained symptomless and his bladder urine sterile.

Discussion

Chronic bacterial prostatitis is a definite clinical entity in which symptoms of urinary discomfort, low back pain, myalgia and arthralgia are accompanied by a positive culture of the prostatic

Table V

Bacteriologic History of D. S., a 31-year-old male

Date	Days on (+) or off (−) drug	Drug	Colonies/ml*				Organism
			1	2	EPS	3	
June 4, 1973	−91	Ampi.	0	0	...	350	*E. coli*
Aug 27, 1973	−175	Ampi.	100,000	100,000	80,000	...	*E. coli*
Sep 4, 1973	+2	Nitrofur.	0	0	0	...	...
Sep 12, 1973	−1	Nitrofur.	0	0	0	...	...
Sep 26, 1973	−15	Nitrofur.	...	100,000	...	...	*E. coli*
Oct 2, 1973	+2	Nitrofur.	...	0	...	...	...
Oct 7, 1973	+7	Nitrofur.	0	...	1,000	...	*E. coli*
Oct 8, 1973	+8	Nitrofur.	0	0	0	...	...
Nov 1, 1973	−2	Nitrofur.	...	0	...	...	...
Nov 30, 1973	−50	Nitrofur.	100,000	100,000	100,000	...	*P. mir.*
Dec 3, 1973	+1	Nitrofur.	0	0	500	...	*P. mir.*
Dec 5, 1973	+3	Nitrofur.	150	300	20,000	...	*P. mir.*
Dec 12, 1973	+10	Nitrofur.	0	0	1,500	...	*P. mir.*
Dec 17, 1973	+1	Cotrim.	0	0	3,300	...	*P. mir.*
Dec 23, 1973	+7	Cotrim.	0	0	350	...	*P. mir.*
Jan 9, 1974	+24	Cotrim.	0	0	1,150	...	*P. mir.*
Jan 23, 1974	+38	Cotrim.	364,000	550,000	20,000	...	*P. mir.*
Feb 8, 1974	+9	Kana.	0	0	0	...	...
Feb 28, 1974	−19	Kana.	0	0	0	...	...
Nov 1, 1974	−264	Kana.	0	0	0	...	...
Sep 29, 1975	−596	Kana.	0	0	0	...	...

Abbreviations used in the table are as follows: 1 = first voided 5 to 10 ml of urine (urethral); 2 = midstream urine specimen (bladder); EPS = expressed prostatic secretion; 3 = first voided 5 to 10 ml of urine after prostatic massage (prostatic). Ampi. = ampicillin; Nitrofur. = nitrofurantoin; Cotrim = cotrimoxazole; Kana. = kanamycin.

* Low counts of Gram-positive organisms (staphylococci, streptococci, diphtheroids) were not included in the Table.

secretion. Physical examination and IVP are usually negative. The organisms isolated are Gram-negative enteric bacteria, as was clearly demonstrated in our patients. As long as the infection in the prostate gland is not eradicated, these patients tend to suffer from relapsing lower and upper urinary tract infections at variable intervals, even if each relapse is adequately treated. In our experience the intervals between recurrent urinary tract infections or positive prostatic secretion cultures vary between a number of days to about 7 months. It is, therefore, reasonable to assume that repeated negative prostatic secretion cultures during the 12 months following adequate treatment can be taken to indicate cure of the chronic bacterial prostatitis. Like the Stanford group (Meares and Stamey, 1968; Stamey, 1972) we have found that, in the absence of any gross pathology of the urinary tract, chronic bacterial prostatitis is the usual cause of recurrent urinary tract infections in the adult male.

The treatment of chronic bacterial prostatitis is difficult, as most of the antibacterial drugs, which are so effective against Gram-negative enterobacteria in urinary tract infections, are not able to cross the lipid membrane of the prostatic epithelium and reach therapeutic levels within the prostatic acini. Investigations in the dog (Winningham *et al.*, 1968; Stamey, Meares and Winningham, 1970; Stamey, 1972), have shown that a drug has to possess lipid solubility, minimal binding to the plasma proteins and a favourable dissociation constant (pKa), producing a high fraction of uncharged molecules in the plasma which are free to cross the prostatic epithelial membrane and diffuse into the prostatic fluid. These uncharged molecules have to pass a pH

Table VI

Bacteriologic History of S. Y., a 56-year-old male

	Days on (+) or off (−)		Colonies/ml*				
Date	drug	Drug	1	2	EPS	3	Organism
May 10, 1972	−12	Ampi.	0	0	...	700	*E. coli*
May 17, 1972	+4	Nitrofur.	0	0	...	150	*E. coli*
June 14, 1972	+32	Nitrofur.	0	0	...	0	...
June 25, 1972	−6	Nitrofur.	600	0	5,000	...	*E. coli*
June 26, 1972	+1	Nitrofur.	0	0	350	...	*E. coli*
July 2, 1972	+4	Cotrim.	0	0	4,000	...	*E. coli*
July 20, 1972	+22	Cotrim.	0	0	...	0	...
Sep 20, 1972	+84	Cotrim.	0	0	30	...	*E. coli*
Oct 30, 1972	+124	Cotrim.	0	0	50	...	*E. coli*
Nov 1, 1972	−1	Cotrim.	0	0	40	...	*E. coli*
Nov 5, 1972	−5	Cotrim.	0	0	100,000	...	*E. coli*
Nov 6, 1972	−6	Cotrim.	200	800	100,000	...	*E. coli*
Nov 8, 1972	+2	Cotrim.	0	0	...	23,000	*E. coli*
Nov 26, 1972	+16	Cotrim.	0	0	0	...	...
Jan 21, 1973	+76	Cotrim.	0	0	90	...	*E. coli*
Apr 1, 1973	+145	Cotrim.	0	0	200	...	*E. coli*
Apr 25, 1973	+13	Strepto.	0	0	0	...	...
May 2, 1973	−7	Strepto.	0	0	0	...	...
July 9, 1973	−75	Strepto.	0	0	0	...	...
July 24, 1973	−90	Strepto.	1,000	0	100	...	*P. mir.*
Jan 1, 1974	−262	Strepto.	6,000	0	1,500	...	*P. mir.*
Mar 24, 1974	−343	Strepto.	500	0	0	...	*P. mir.*
Apr 23, 1974	−373	Strepto.	0	0	0	...	...
June 10, 1974	−420	Strepto.	200	0	0	...	*P. mir.*
Oct 10, 1974	−546	Strepto.	0	0	0	...	...
Feb 14, 1975	−669	Strepto.	3,400	0	700	...	*P. mir.*
Apr 14, 1975	−728	Strepto.	0	0	0	...	...
June 23, 1975	−798	Strepto.	1,000	0	200	...	*P. mir.*
Nov 25, 1975	−953	Strepto.	0	0	0	—	—

Abbreviations used in the table are as follows: 1 = first voided 5 to 10 ml of urine (urethral); 2 = midstream urine specimen (bladder); EPS = expressed prostatic secretion; 3 = first voided 5 to 10 ml of urine after prostatic massage (prostatic). Ampi. = ampicillin; Nitrofur. = nitrofurantoin; Cotrim. = cotrimoxazole; Strepto. = streptomycin.

gradient between the plasma (7·4) and the prostatic fluid (6·6), where they become ionised (ion-trapping phenomenon) and as such cannot cross back into the plasma, and consequently concentrate in the prostate. As a result of these conditions, acids cannot exceed their plasma concentration in the prostatic fluid, whereas bases may theoretically reach a concentration in the prostate many times that in the plasma.

Trimethoprim (TMP), enhanced in its antibacterial activity by combination with sulphamethoxazole (SMZ), was heralded as meeting all the criteria for adequate concentration in the prostate (Bushby, 1969; Carroll *et al.*, 1971); it is a lipid soluble base, has a protein binding of 45% and a pKa of 7·3 thus allowing over 50% of its molecules in the plasma to be uncharged and free to diffuse into the prostate. However, the few small clinical trials reported till now indicate that cotrimoxazole (80 mg of TMP+400 mg of SMZ) in chronic bacterial prostatitis is not as effective as had been expected. In a series of such cases presented by Stamey (1972), no cure was obtained in 2 of 11 patients treated for 2 weeks with this drug. In another series of 13 such patients, treated similarly, only 2 patients were cured (Meares, 1973). When the treatment period with the same drug was lengthened to 12 weeks, 5 out of 16 patients were permanently cured (Meares, 1975).

In our own 6 patients short periods of treatment with cotrimoxazole of between 10 and 30 days (first 5 days 160 mg of TMP+800 mg of SMZ, b.i.d.; and then 80 mg of TMP+400 mg of SMZ, b.i.d.) never succeeded in curing the prostatic infection, although in some it brought about the temporary sterilisation of all the 3 divided samples (E. P., Table I; U. Z., Table II; A. Y., Table IV; D. S., Table V). The longest sterilisation period reached was about 6 months in patient E. P. (Table I).

All 6 patients were then given cotrimoxazole for at least 4 months (160 mg of TMP+800 mg of SMZ, b.i.d., for the first 10 days and 80 mg of TMP+400 mg of SMZ, b.i.d., for the rest of the period). In 2 of them (E. P., U. Z.) this treatment resulted in a permanent cure. The minimal follow-up period was 27 months. In patient M. K. (Table III) sterilisation of the prostatic fluid was also obtained after a similar treatment but this patient was lost to our follow-up a month after stopping the treatment, when all the cultures were sterile. In patient A. Y. (Table IV) more than 8 months of uninterrupted daily cotrimoxazole resulted in an apparent cure but almost 7 months later the culture of the prostatic fluid again yielded growth of *E. coli* as before the treatment. Patient D. S. (Table V) developed an acute bladder infection on the 38th day of the cotrimoxazole treatment, which had to be stopped. In patient S. Y. (Table VI) two 4-month trials of cotrimoxazole did not result in sterilisation of the prostatic secretion. All the pathogens in our patients were as sensitive to cotrimoxazole after the long-term treatment as before it, so that the failure of this drug to eradicate the prostatic infection cannot be explained by the appearance of resistant strains.

The failure of cotrimoxazole to cure the chronic prostatic infection in 3 out of our 6 patients may be explained by the fact that the TMP concentration in the prostate is not as high in man as in the dog (Fowle and Bye, 1971; Nielsen and Hansen, 1972; Reeves, 1974). Furthermore, recent research has shown that the pH of the prostatic fluid in older men is around 7·6 (Fair, 1975) and not 6·6 as in the dog. At such a pH, TMP will no longer be able to concentrate adequately within the prostate and may even reach a higher concentration in the plasma. The failure of the short-term cotrimoxazole treatment to cure chronic bacterial prostatitis and the effectiveness of the long-term treatment with the same drug may be explained by the finding (Blacklock and Beavis, 1974) that the pH of inflamed prostatic tissue is high (7·4 to 8) but that the levels return gradually to about 6·6 with the passage of time, as the inflammatory reaction wanes. TMP is then able to reach higher concentrations in the prostate, which are adequate to cure the chronic prostatic infection.

In view of the failure of cotrimoxazole to cure chronic bacterial prostatitis in 3 out of our 6 patients (A. Y., D. S. and S. Y.) and also in the majority of the patients presented by Stamey and Meares (Stamey, 1972; Meares, 1973; Meares, 1975), we considered the use of other antibacterial drugs effective against Gram-negative enterobacteria when given parenterally, even if theoretical considerations indicate that they should not be able to cross the prostatic epithelium. This had already been reported in a patient, who after repeated unsuccessful trials with different antibacterial drugs, was permanently cured of his chronic bacterial prostatitis after treatment with kanamycin for 5 days (500 mg, i.m., b.i.d.) (Stamey, 1972).

Kanamycin is a lipid insoluble base and therefore theoretically not able to cross the normal prostatic epithelium. However, it is not bound to plasma proteins and has a favourable pKA of 7·2. After an i.m. injection of 1·0 g it reaches levels of 20 to 35 μg/ml in the plasma, which are sufficient to kill many of the Gram-negative enterobacteria found in urinary tract infections. If it were lipid soluble kanamycin could reach a therapeutically effective concentration in the prostate even at the pH of 7·4. It was given to patients A. Y. (Table IV) and D. S. (Table V) for 14 and 10 days respectively (1,000 mg, i.m., b.i.d. for the first 3 days and 500 mg, b.i.d., for the rest of the period) with a resulting permanent cure of the chronic bacterial prostatitis. Patient

S. Y. (Table VI) received streptomycin (33% protein-bound with a high potency at a pH 7 to 8) for 12 days at a dose of 1 g, i.m., daily and the prostatic infection with *E. coli* was cured; no further urinary symptoms or bladder infections have occurred since the last treatment with streptomycin, in spite of sporadic growth of small numbers of *P. mirabilis* preponderant in the urethral culture. In all 3 of these patients the follow-up was for at least 19 months.

Conclusions

Although theoretically cotrimoxazole should be the most effective drug in the cure of chronic bacterial prostatitis, it has not been able to achieve this in the majority of the reported cases. In our experience kanamycin and streptomycin were no less effective. Of 6 patients, 4 were definitely cured (2 by cotrimoxazole and 2 by kanamycin) and 2 probably cured (1 by cotrimoxazole and 1 by streptomycin). Cotrimoxazole was effective only when given for a period of at least 4 months, whereas kanamycin and streptomycin cured the prostatic infection within 10 to 14 days. In view of this success with lipid insoluble kanamycin and streptomycin and the recent finding that the pH of human prostatic secretion is higher than was previously believed, other antimicrobials should be reconsidered in the treatment of chronic bacterial prostatitis.

Summary

6 cases with chronic bacterial prostatitis were reviewed. The effort and patience required to diagnose this condition accurately by means of differential urine and prostatic secretion cultures is extremely worthwhile.

Cotrimoxazole, which has been suggested as a most effective antibacterial drug in chronic bacterial prostatitis, cured only 3 out of our 6 patients and then only after continuous treatment for 4 months. 2 of the remaining patients were cured by a 10 to 14 days' course of kanamycin and the third was probably cured by streptomycin. On theoretical grounds neither of these lipid insoluble drugs should be capable of penetrating the prostatic epithelium.

The implications of these findings are discussed.

References

Blacklock, N. J. and Beavis, J. P. (1974). The response of prostatic fluid pH in inflammation. *British Journal of Urology*, **46**, 537-542.

Bushby, S. R. M. (1969). Combined antibacterial action *in vitro* of trimethoprim and sulfonamides: the *in vitro* nature of synergy. *In:* The synergy of trimethoprim and sulphonamides. *Postgraduate Medical Journal*, **45** (Suppl.), 10-18.

Carroll, P. T., Robb, C. A., Tippett, L. O. and Langston, J. B. (1971). Antibacterial activity of diaveridine, trimethoprim, and selected sulfonamides in prostatic fluid. *Investigative Urology*, **8**, 686-694.

Fair, W. R. (1975). Personal communication.

Fowle, A. S. E. and Bye, A. (1971). Concentration of trimethoprim and sulphamethoxazole in human prostatic fluid. *Proceedings of the 7th International Congress of Chemotherapy, Prague*. Prague, Avicenum, 1972, 1289-1290.

Meares, E. M. and Stamey, T. A. (1968). Bacteriologic localisation patterns in bacterial prostatitis and urethritis. *Investigative Urology*, **5**, 492-518.

Meares, E. M., Jr. (1973). Observations on activity of trimethoprim-sulphamethoxazole in the prostate. *Journal of Infectious Diseases*, **128** (Suppl.), S679-S685.

Meares, E. M. (1975). Prostatitis, a review. *Urologic Clinics of North America*, **2**, 3-27.

Nielsen, M. L. and Hansen, I. (1972). Trimethoprim in human prostatic tissue and prostatic fluid. *Scandinavian Journal of Urology and Nephrology*, **6**, 244-248.

Reeves, D. S. and Ghilchik, M. (1970). Secretion of the antibacterial substance trimethoprim in the prostatic fluid of dogs. *British Journal of Urology*, **42**, 66-72.

REEVES, D. (1974). Personal communication. Quoted by Blacklock, N. J. and Beavis, J. P.
STAMEY, T. A., GOVAN, D. E. and PALMER, J. M. (1965). The localisation and treatment of urinary tract infections: the role of bactericidal urine levels as opposed to serum levels. *Medicine*, **44**, 1-36.
STAMEY, T. A., MEARES, E. M., Jr. and WINNINGHAM, D. G. (1970). Chronic bacterial prostatitis and the diffusion of drugs into prostatic fluid. *Journal of Urology*, **103**, 187-194.
STAMEY, T. A. (1972). *Urinary Infections*. First edition. Baltimore: Williams and Wilkins, pp. 161-212.
WINNINGHAM, D. G., NEMOY, N. J. and STAMEY, T. A. (1968). Diffusion of antibiotics from plasma into prostatic fluid. *Nature*, **219**, 139-143.

The Authors

A. Pfau, MD, FACS, Associate Professor of Urology.
T. Sacks, MMed(Path), FRCPath, Associate Professor and Chairman of the Department of Clinical Microbiology.

Requests for reprints: A. Pfau, MD, Department of Urology, Hadassah University Hospital, P.O.B. 499, Jerusalem, Israel.

British Journal of Urology (1976), **48**, 254 ©

Short Case Report

An Osteolytic Lesion as a Presentation of Bladder Carcinoma

A case of transitional cell carcinoma presenting as an osteolytic lesion in the calcaneum is most unusual.

Case Report

A 67-year-old woman fell and injured her right ankle. This was treated as a simple sprain and the initial radiographs were essentially normal. She developed increasing pain and tenderness with signs of local inflammation. This was thought to be due to osteomyelitis and abscess formation. 2 months after the initial radiographs, further films showed a large osteolytic lesion (Fig. 1). It was explored and curettings sent for histological examination. This revealed sheets of cells some of which showed squamous metaplasia. The patient's history was reviewed in the search for a primary growth and on further questioning she admitted to some episodes of dysuria and on one occasion haematuria. Excretion urography was performed and a filling defect demonstrated in the bladder. Cystoscopy and biopsy confirmed the presence of a large papillary transitional cell carcinoma with superficial invasion. The histology of the bladder tumour and the metastatic deposit (Fig. 2) had the same cellular pattern. The patient underwent a below-knee amputation precipitated by a profuse haemorrhage after the biopsy. The bladder lesion was treated by megavoltage X-Ray therapy.

Comment

It is uncommon for bladder carcinoma to present as a metastatic deposit. This is a late feature since spread is related to the degree of invasion of the bladder wall and histological grade. Spread from the bladder wall is then usually by the local lymphatics and venous plexuses to the vertebral column, pelvis, skull, ribs and humerus (Mullin, Glenn and Paulson, 1975). This case is unusual in the lack of urological symptoms and site of the deposit. Bladder carcinoma may produce an osteoblastic lesion but are more commonly osteolytic and respond well to radiotherapy. This was not possible in this case since the secondary haemorrhage had necessitated an amputation.

J. G. W. FEGGETTER
Department of Urology, Newcastle General Hospital

Reference

MULLIN, E. M., GLENN, J. F. and PAULSON, D. F. (1975). Lesions of bone and bladder cancer. *Journal of Urology*, **113**, 45-46.

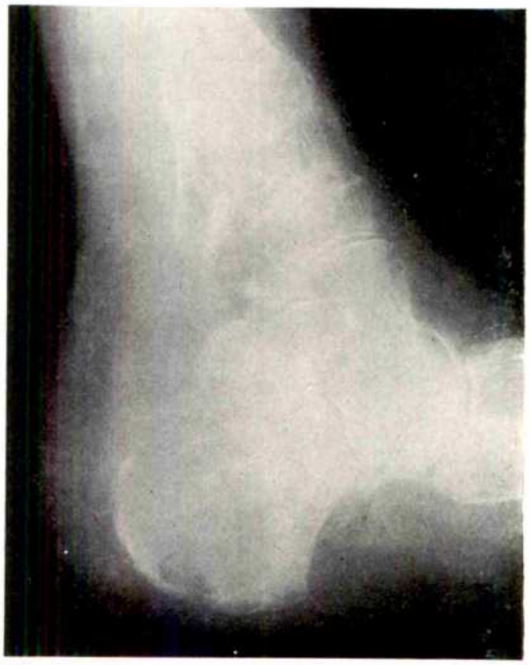


Fig. 1

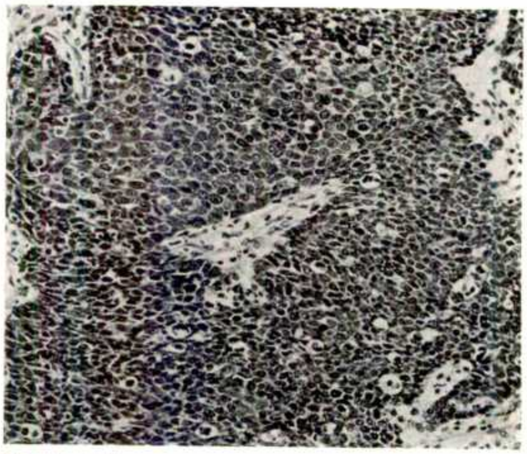


Fig. 2. × 160.

British Journal of Urology (1976), **48**, 255-263 ©

The Use of Alpha-adrenergic Blockers in Benign Prostatic Obstruction

MARCO CAINE, ALPHONSE PFAU and SHAUL PERLBERG
Department of Urology, Hadassah University Hospital, Jerusalem, Israel

There has been much interest in recent years in the role played by the adrenergic receptors in the urinary tract and a certain amount of work has been done in our department on this subject. Amongst other investigations we have studied the adrenergic receptors in the rat prostate (Raz, Zeigler and Caine, 1973) and subsequently in the human prostate (Caine, Raz and Zeigler, 1975). The latter was performed on tissue obtained from patients undergoing operations for benign prostatic obstruction, and separate studies were made of the receptors in the prostatic capsule, the enucleated "adenoma" and selected parts of the bladder neck and trigone. It was found that the prostatic capsule was extremely rich in α-adrenergic receptors, the prostatic adenoma moderately rich and the bladder neck region showed variable results, the maximal α-receptor response being in the region of the trigone. In the case of the rat prostate there was evidence of additional β-adrenergic activity but for practical purposes this was negligible in the human material.

As a consequence of the above findings, and having regard to known clinical and pharmacological causative factors, it was suggested in those papers that certain cases of acute retention of urine in patients with benign hypertrophy of the prostate may be due to sudden stimulation of the α-adrenergic receptors, causing an increase in tone of the smooth muscle tissue in the prostate and prostatic capsule, hence resulting in an increase in the closure pressure on the urethra. Further consideration suggested that if this be the case, variations in α-adrenergic activity of lesser degree might be responsible for at least some of the variations in the severity of the obstructive symptoms, which is so typical of many patients suffering from prostatic enlargement. As a corollary, if this hypothesis be true, one could anticipate a beneficial effect from the use of α-adrenergic blocking agents in such patients with retention or obstructive symptoms. It was accordingly decided to carry out a trial of such agents, to see if they would be of help to these patients.

During the course of the trial it soon became evident that the majority of the patients were deriving considerable benefit from the treatment and that they fell into a number of clinical groups, which will be discussed below. A few illustrative cases from the different groups will be briefly described.

Illustrative Cases

Case A

S. K., 73 years old, with typical symptoms due to a 50 g benign enlargement of the prostate of some years' duration, attended urgently with virtually complete urinary retention. On straining, he was able to pass only a few drops of urine (Fig. 1a) and the bladder was tense and palpable half-way to the umbilicus. Immediately following a slow intravenous injection of phentolamine (10 mg) he was able to pass 180 ml of urine in a stream, at the rate of 10 ml per sec (Fig. 1b). A few minutes later he passed a further 90 ml in a stream. He was started on oral phenoxybenzamine, 10 mg b.d., and during the 6 weeks since the acute episode he has had no further urinary difficulties (Fig. 1c).

Case B

S. A., a 57-year-old tourist, had been complaining of mild disturbances of micturition due to an enlarged prostate for the past year. The previous day complete acute retention had supervened and 800 ml of urine had been removed by catheterisation. When seen the following day he was in complete retention again, with a palpable, tense bladder.

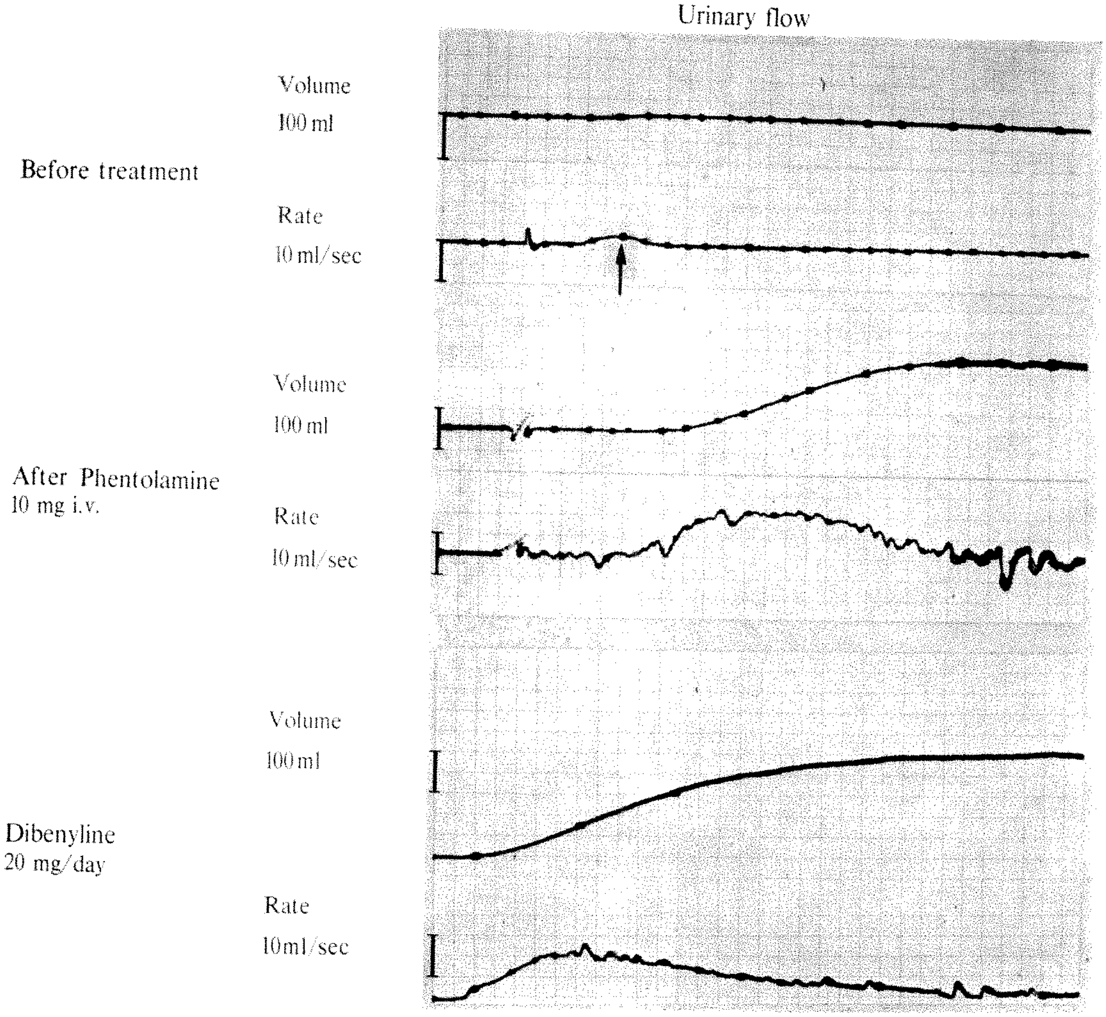


Fig. 1. Case A: (a) Virtually complete retention. Only a few drops passed, as indicated by arrow; (b) 180 ml passed at rate of 10 ml/sec following injection of phentolamine; (c) 250 ml passed with satisfactory flow 1 week later whilst receiving Dibenyline. (Irregularities in flow-rate recording caused by patient touching receptacle).

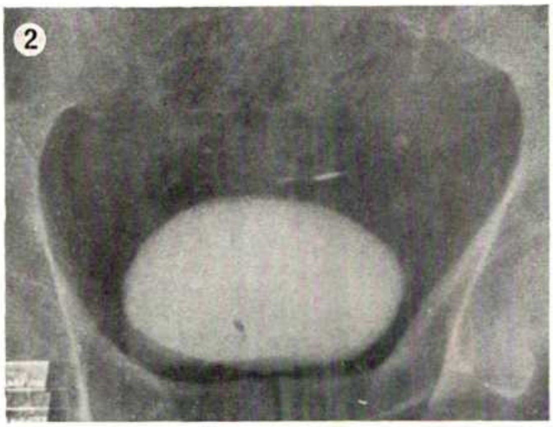
Following an intravenous injection of 10 mg phentolamine he immediately passed a stream of 80 ml of urine, with considerable symptomatic relief, although it was clear that he was not emptying his bladder. Phenoxybenzamine, 10 mg b.d. by mouth, was immediately started and within 24 hours the patient was urinating freely again and was able to return to his own country for further treatment.

Case C

H. W., 60 years old, had a history of increasing difficulty in micturition for the past 1½ years. This had recently become much worse and during the 4 weeks prior to consultation he had 6 episodes of acute retention, each of which had necessitated catheterisation or suprapubic aspiration of the bladder. Rectal examination revealed a benign enlargement of the prostate and IVP showed a normal upper urinary tract and only 20 ml residual urine. Administration of phenoxybenzamine 10 mg a day was commenced, with considerable improvement in the patient's micturition and no further attacks of acute retention occurred during the subsequent 2 months up to his operation and removal of a 50 g benign prostate.

Case D

H. B., a 55-year-old patient, had been suffering for years from urinary disturbances as a result of a 40 g benign



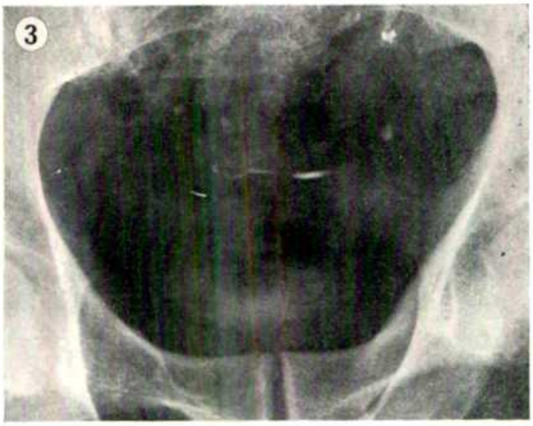


Fig. 2. Case E: Post-voiding cystogram before therapy.

Fig. 3. Case E: Post-voiding cystogram whilst receiving Dibenyline.

enlargement of the prostate. Every 1-2 months he had an attack of acute urinary retention necessitating catheterisation. Immediately prior to his being seen, he had had 3 attacks of acute retention, each necessitating catheterisation. When seen, he was again in acute retention. 10 mg phentolamine were given intravenously, immediately following which he was able partly to empty his bladder with a moderate stream. Oral phenoxybenzamine, 10 mg b.d., was commenced and the patient started to urinate freely without any further difficulties. On one of the following days the patient forgot to take his medication and marked difficulty with micturition reappeared. He took 20 mg of phenoxybenzamine at one time and 3 hours later was able to empty his bladder with ease. The patient does not wish to undergo operation and has continued to receive the phenoxybenzamine for the past 6 months. During this period he has had no further attacks of acute retention and the prostatic symptoms have been minimal.

Case E

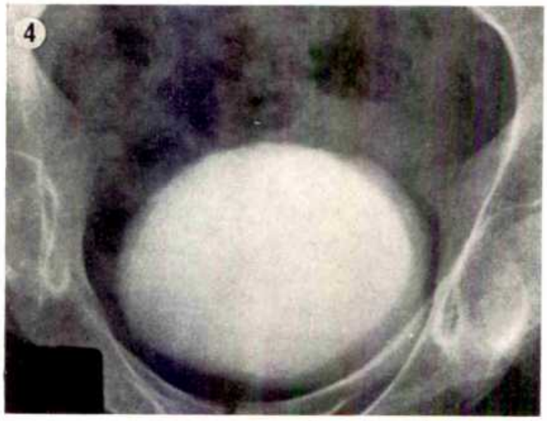
D. A., 65 years old, was seen in the out-patient department at the end of February 1974 because of frequency and difficulty in micturition for the last few years. 2 weeks previously an indwelling catheter had been inserted because of acute urinary retention. The catheter was removed after a week but the patient continued to urinate with difficulty. Bimanual examination revealed a non-tender, firm, smooth enlargement of the prostate of about 30 g. The IVP showed good function of both kidneys; the bladder was trabeculated and there was a residual urine of about 80 ml after micturition (Fig. 2). Phenoxybenzamine was administered, 10 mg t.i.d. and a marked symptomatic improvement occurred in the micturition. A repeat IVP, 6 months later, revealed that the bladder now emptied completely (Fig. 3). The patient has now been receiving the same treatment for 1 year with maintained symptomatic relief.

Case F

M. O., a 52-year-old man, was repeatedly seen in our out-patient department on account of hesitancy, difficulty, frequency and dysuria. In 1971 he had undergone a litholapaxy for 3 bladder stones. Physical examination revealed a smooth, firm enlarged prostate of about 30 g. An IVP performed in January 1974 showed good secretion from both kidneys and there was a residual urine of about 100 ml after micturition (Fig. 4). Treatment with phenoxybenzamine, 10 mg a day, was started and immediate improvement occurred in his micturition. This improvement was accompanied by some postural hypotension and the dosage was therefore reduced to 10 mg every other day, with the same beneficial effect on micturition but without postural hypotension. A repeat IVP in August 1974 now revealed almost no residual urine in the post-voiding cystogram (Fig. 5). The patient continues to receive the same treatment, with maintained benefit.

Case G

Y. H., 60 years old, had been complaining for almost 18 months of hesitancy, weak and intermittent urinary stream and terminal dribbling. Physical examination revealed a slightly enlarged prostate of about 15 g. The IVP showed good secretion from both kidneys and a slightly trabeculated bladder with a small amount of residual urine. Uroflowmetry demonstrated a maximal flow rate of only 10 ml per second and protracted micturition (Fig. 6a). The patient was started on phenoxybenzamine, 10 mg daily and 2 weeks later uroflowmetry showed an increased flow rate and a shortening of the bladder emptying time (Fig. 6b). The dose was increased to 20 mg a day, with further marked symptomatic improvement and the patient remarked that he was now urinating as in his youth.



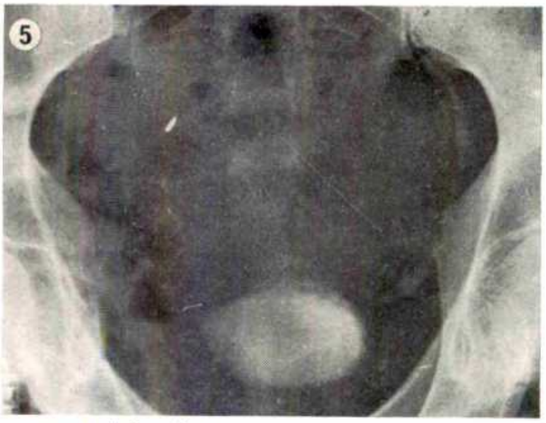


Fig. 4. Case F: Post-voiding cystogram before therapy.

Fig. 5. Case F: Post-voiding cystogram whilst receiving Dibenyline.

Uroflowmetry now showed a doubling of the flow rate to 20 ml per second, as compared to that before treatment and a rapid emptying of the bladder (Fig. 6c).

Case H

S. K., a 65-year-old patient, complained of recent weakening of his urinary stream. Rectal examination revealed an enlarged benign prostate. The IVP showed good secretion from both kidneys and the bladder emptied with a small residual urine. Uroflowmetry demonstrated a maximal flow rate of 8 ml per sec and the patient could not pass more than 80 ml at one time (Fig. 7a). After administration of 10 mg phenoxybenzamine once a day, the patient felt considerable improvement in his micturition and uroflowmetry showed a doubling of the maximal urine flow rate (Fig. 7b) and the ability to void 200 ml at one time.

Case I

Y. G., 62 years old, had been under observation in our out-patient department for 4 years on account of hesitancy, terminal dribbling, frequency and urgency. There was a past history of a myocardial infarct in 1969 but there were no residual cardiac symptoms. Rectal examination revealed an enlarged benign prostate of about 30 g in size. The IVP showed good secretion from both kidneys and the bladder emptied with a small amount of residual urine. Symptomatic treatment did not improve the patient's condition and in June 1974 the difficulties in micturition increased. Uroflowmetry revealed a slow and protracted emptying of the bladder, the maximum flow rate being 10 ml per sec (Fig. 8a). The patient was started on phenoxybenzamine, 10 mg once a day, and an immediate improvement occurred in his micturition. The micturition was easier, the frequency diminished and the patient was able to urinate every 3 hours during the day and only once during the night. Repeat uroflowmetry demonstrated an increase in the urine flow rate up to 17 ml per second and the urine volume passed at one time was appreciably increased (Fig. 8b). The patient has now been taking phenoxybenzamine, 10 mg once a day for 6 months, without any side effects and with maintained benefit.

Discussion

The illustrative cases recorded above represent a small selection from more than 50 cases of benign prostatic enlargement we have treated up to date and there is clear evidence of a pronounced beneficial effect in a large proportion of them. In the case of patients already in complete retention or on the verge thereof (*e.g.* cases A and B), the immediate passage of urine following administration of the α-blocker and the avoidance of the necessity for catheterisation afford good objective evidence of the efficacy of the treatment. In patients suffering from obstructive symptoms but without acute retention, reliance was not placed on the patients' subjective improvement alone (which is notoriously fallacious) but on objective observations such as a diminution of residual urine in the IVP (*e.g.* cases E and F), or an improvement in the urinary flow rate as shown on uroflowmetry recordings (*e.g.* cases G, H and I).

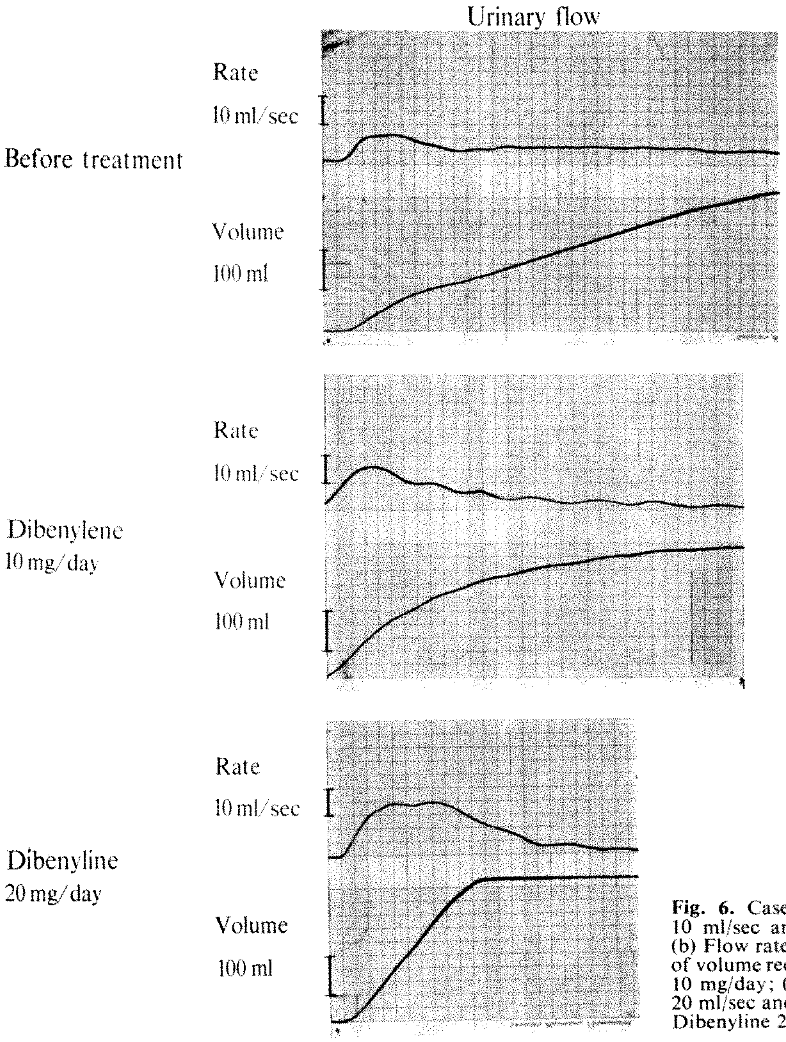


Fig. 6. Case G: (a) Maximal flow rate of 10 ml/sec and slowly accumulating volume; (b) Flow rate increased to 15 ml/sec and slope of volume recording improved with Dibenyline 10 mg/day; (c) Flow rate increased further to 20 ml/sec and total volume passed rapidly with Dibenyline 20 mg/day.

In the course of evaluating the treatment it became evident that the patients tended to fall into a number of groups and it is convenient to discuss the various aspects of the treatment and the results in relationship to each of these groups.

(a) Cases with Acute Retention. At the outset we would stress once again what we have already stressed in the past, namely, that we do *not* suggest that all cases of acute retention of urine are due to over-stimulation of the α-adrenergic receptors and are therefore potentially reversible. There is no doubt that other causes exist and we can therefore hope for benefit from α-blockers in only a percentage of cases. It may also be that once complete retention is established, with overstretching of the bladder detrusor fibres, a mechanical factor is added to the physiological mechanism which originally initiated it and the retention may no longer be reversible by blocking that mechanism. Perhaps for these reasons our success with this treatment was least in this group of cases. None-the-less, in 5 out of 8 cases, micturition was re-established following administration of an α-blocker without the need for catheterisation. From the above considerations it could be

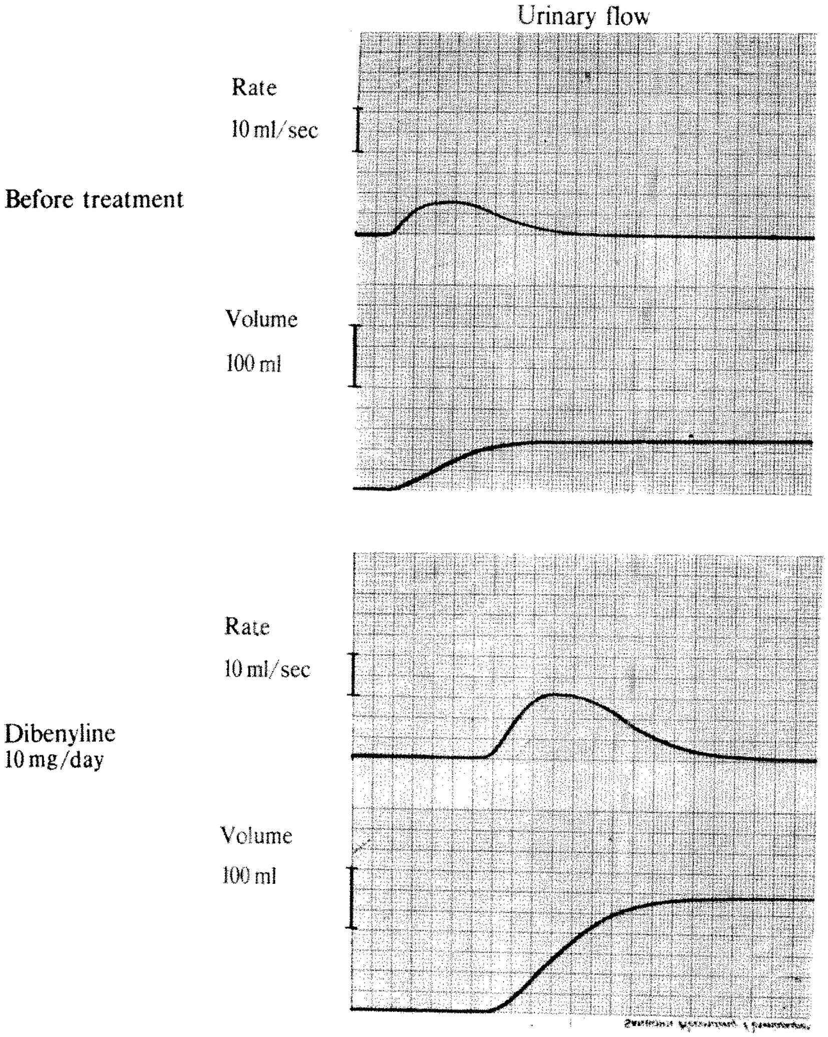
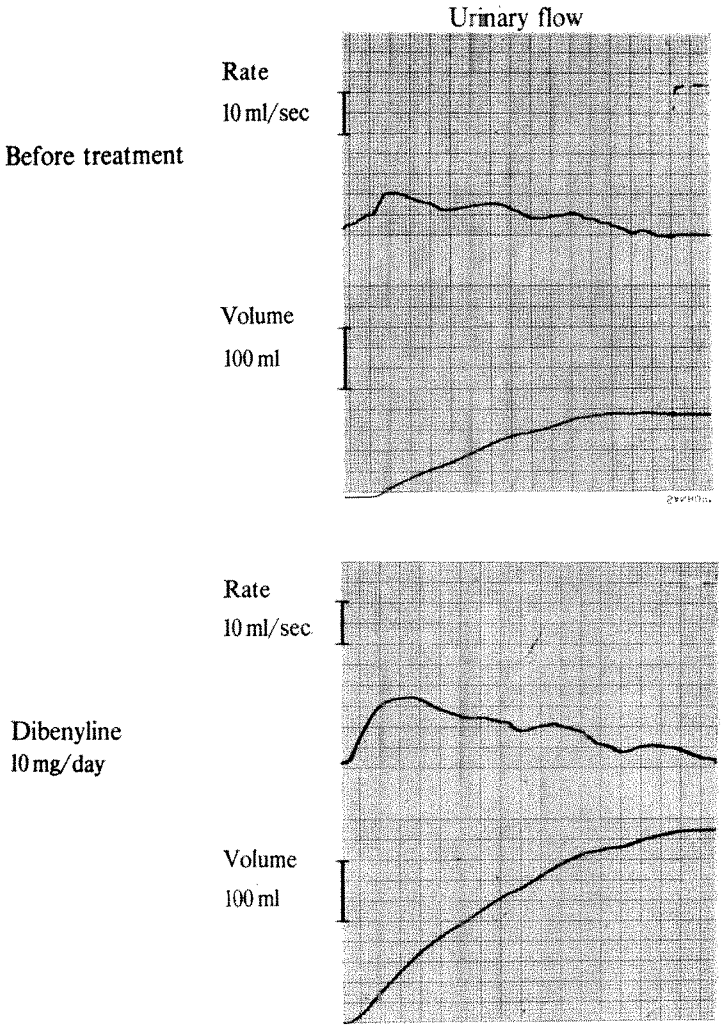


Fig. 7. Case H: Maximum flow rate improved from 8 to 16 ml/sec and larger volume passed more rapidly after administration of Dibenyline 10 mg/day.

anticipated that the best results would be obtained by treating these patients in the incipient or initial stage of the retention, before over-stretching of the detrusor has occurred. In such cases it seems logical to choose a quick-acting blocker and give it parenterally, so as to obtain as rapid an effect as possible; and for this reason phentolamine (Regitine) by the intravenous route was chosen, as illustrated by patients A and B. However, in 2 patients on the verge of retention, who were still able to pass a few drops, administration of Dibenyline alone produced a sufficiently rapid result to enable them to pass urine satisfactorily again. Following relief of the acute retention we have usually continued and reinforced treatment with a longer-acting oral preparation.

(b) Cases with Recurrent Acute Retentions. A number of patients are encountered who develop recurrent acute retentions of urine at frequent intervals. In such cases one may hope to prevent



MEDICINE

Fig. 8. Case I: Maximum flow rate improved from 10 ml/sec to 17 ml/sec and larger volume passed more rapidly after administration of Dibenyline 10 mg/day.

the occurrence of further attacks of acute retention by maintaining the patient on prophylactic treatment with an α-blocker, as is illustrated by patients C and D (in case D, an attack of acute retention was also aborted). It is naturally difficult to bring objective scientific proof of the efficacy of the treatment in such a case, for it may be argued that the patient would not have had further attacks of acute retention in the given period, even if he had not received the treatment. However, the apparently clear and impressive effect in such patients as the above, taken together with the objectively demonstrated therapeutic effect in the other groups, does give strong evidence of a prophylactic value in this group of cases.

(c) Cases with Obstructive Symptoms. As mentioned above, one of the typical observations in prostatic patients is the variability of their symptoms and it was considered that these may be due, in part at least, to variations in the α-adrenergic activity affecting the smooth muscle of the prostate, prostatic capsule, bladder neck and posterior urethra and as a corollary, that it should prove possible to improve these symptoms by α-adrenergic blockade. In this case it is evident that a relatively long-acting α-blocker is required and phenoxybenzamine (Dibenyline) was accordingly chosen. The dose given was 10 mg, once or twice a day, rarely increased to 3 times a day. A large majority of these patients reported marked subjective relief of their symptoms, with an improved flow, less hesitancy and less frequency. However, as these subjective evaluations in prostatic patients are notoriously extremely unreliable, we wished to obtain more objective evidence of improvement. As discussed in another paper (Caine, Perlberg and Gordon, 1975) the two most reliable parameters for such assessment appear to be the amount of residual urine and the measurement of the urinary flow rate. The former was performed in a number of patients and objective evidence of a diminution was obtained (*e.g.* cases E and F). However, the simplest method in practice was the flowmetry, an examination we have been carrying out almost routinely in our clinic for the last few years. Formerly we used a 2-channel Hewlett-Packard recorder, as seen in most of the charts reproduced, and more latterly we have been using an 8-channel Elema-Schönander Mingograph recorder which, with the associated special flow-meter transducer and amplifier, is more sensitive and affords the opportunity of a wider variety of studies. As illustrated in the above cases (G, H and I), we were able to obtain good objective evidence of an increased flow rate and also the ability to pass a larger quantity of urine (indicating less frequency) following the administration of phenoxybenzamine.

The flow rate depends upon two factors, namely the expulsive force of the bladder and the resistance of the outflow tract. Any effect of an α-adrenergic blocker on the bladder would be to diminish the tone rather than to increase it, since it would then leave the β-receptors, which predominate in the dome of the bladder (Edvardsen and Setekleiv, 1968), with a relatively unopposed effect. It is clear, therefore, that the α-blockers must produce their beneficial effect upon the outflow tract and this, in the case of patients suffering from obstructive prostatic symptoms, will be predominantly on the enlarged prostate and its capsule.

Side Effects and Contraindications

Insofar as the dosage of phenoxybenzamine necessary to produce a satisfactory response has been relatively small, namely 10-20 mg per day (rarely 30 mg per day), the side effects met with have been minimal. They have consisted of dizziness and palpitation in a few patients and a number of the younger patients have reported an absence of external ejaculation of semen. These effects are explicable by other α-blocking effects on the vascular system and on the bladder neck and are rapidly reversible on stopping the treatment. One might anticipate more marked side effects from the relatively high dose of phentolamine given in an attempt to overcome incipient acute retention. The injection is given with the patient lying down, careful watch is kept on the blood pressure and he is allowed to resume the erect position only slowly and under supervision. With this regime no trouble has been encountered, only 1 patient complaining of nasal stuffiness —a recognised reaction to α-adrenergic blockade.

Because of the effect of α-adrenergic blockers on the cardiovascular system it is probably advisable to avoid their use in patients suffering from recent myocardial infarction, heart failure or advanced cerebral arteriosclerosis.

The Indications for Treatment with Alpha-adrenergic Blockers

At the outset we would stress the fact that the use of α-adrenergic blockade in the prostatic patient is in no sense a treatment of the prostatic enlargement itself but is suggested as a purely symptomatic treatment to relieve some of the obstructive features of the condition. Its effect is entirely temporary, generally passing off within a few days after ceasing treatment. The indications for its use, according to our experience up to date, may be summarised as follows:

(*a*) In patients with incipient, or sometimes in established, sudden acute retention—in order to obviate the necessity for catheterisation.
(*b*) In patients with repeated attacks of acute retention—as a prophylactic to prevent further attacks until operation be performed.
(*c*) In patients with symptoms, who otherwise do not need prostatectomy—for symptomatic relief.
(*d*) In patients with exacerbation of prostatic symptoms immediately after other unrelated operations or illness—to tide them over the acute phase until prostatectomy can be performed.
(*e*) In patients with an indwelling catheter following urinary retention—to free them from the catheter. This is a group in whom it is not possible to bring objective scientific evidence, for many patients will spontaneously start passing urine again after removal of the catheter, without any therapy. However, a number of patients who have been unfit for or have refused operation, in whom repeated attempts to remove an indwelling catheter had failed, have been able to dispense with their catheters following the commencement of phenoxybenzamine treatment.

Summary

As a result of previous *in-vitro* studies on the α-adrenergic receptor activity of the human prostate and prostatic capsule a trial was made of α-adrenergic blockers for the relief of obstructive prostatic symptoms.

Considerable benefit was obtained in several groups of patients, as demonstrated either by the relief or prevention of complete retention, or by diminution in residual urine or improvement in urinary flow-rate recordings. A number of illustrative cases are described, and the indications for the use of this treatment are suggested.

It is emphasised that this treatment provides symptomatic relief only, and in no sense purports to be a treatment of the enlarged prostate itself.

References

Caine, M., Perlberg, S. and Gordon, R. (1975). The treatment of benign prostatic hypertrophy with Flutamide (SCH. 13521): a placebo-controlled study. *Journal of Urology*, **114**, 564-568.

Caine, M., Raz, S. and Zeigler, M. (1975). Adrenergic and cholinergic receptors in the human prostate, prostatic capsule and bladder neck. *British Journal of Urology*, **47**, 193-202.

Edvardsen, P. and Setekleiv, J. (1968). Distribution of adrenergic receptors in the urinary bladder of cats, rabbits and guinea-pigs. *Acta Pharmacologica et Toxicologica*, **26**, 437-445.

Raz, S., Zeigler, M. and Caine, M. (1973). Pharmacological receptors in the prostate. *British Journal of Urology*, **45**, 663-667.

The Authors

Marco Caine, MS, FRCS, Professor of Urology and Head of Department.
Alphonse Pfau, MD, Associate Professor of Urology.
Shaul Perlberg, MD, Assistant Physician.

OF MEDICINE
LIBRARY

British Journal of Urology (1976), **48**, 264 ©

Short Case Report

Posterior Urethral Duplication

Although urethral duplication is a well recognised congenital anomaly it is very unusual for the accessory channel to open into the perineum or anal canal itself (Williams and Bloomberg, 1975).

Case Report

A West Indian boy with nocturnal enuresis presented at the age of 7 with a 6-month history of day-time wetting. He had begun to sit down to micturate and was thought by his parents to pass urine through the anus. Examination showed a healthy boy with bilateral undescended testicles and a dorsally placed external urinary meatus of pin-hole calibre.

An IVP was normal. Spina bifida occulta of L5, S1, vertebrae was noted. An MSU yielded a significant growth of *E. coli*. Under anaesthetic the stenosed external meatus required dilatation, the narrowing was found to extend back to the coronal level. From this point the urethra was of normal calibre to the base of the penis where an unnegotiable stricture was encountered. Sigmoidoscopy revealed the lower end of a duplex colon at the recto-sigmoid junction. Descending urethrography, via a suprapubic catheter, showed a normal bladder and proximal urethra to the level of the external sphincter but the child was unable to micturate.

A first-stage, posteriorly based, skin flap urethroplasty was performed. No communication between the urethra and the bowel was found on this occasion. 10 days later, when a leak of urine through the anus was observed, a further search was made. Methylene blue was inserted until the bladder was fully distended and a leak of dye via the anus led to the location of an orifice just inside the anterior anal margin (Fig.). A sound was passed easily through this channel to enter the bladder inside the bladder neck at the 5 o'clock position. This ectopic tract was dissected from the anal margin to the bladder neck and excised. Histology showed a tubular structure lined with transitional cell epithelium and surrounded by a wall of smooth muscle and fibrous tissue. There were many accessory transitional cell-lined ducts in the wall.

6 months later a routine second-stage skin implant urethroplasty was performed after further dilatation of the meatal stricture. Following this procedure the boy was able to micturate with an excellent stream and normal control. He has required no further dilatation and micturition remains normal 2 years after surgery.

Comment

The most unusual feature illustrated by our patient was the late onset of anal micturition presumably due to increasing stenosis of the normally sited and partially strictured urethra.

D. OSBORNE and J. C. GINGELL
Royal Free Hospital London and Southmead Hospital, Bristol

Reference

WILLIAMS, D. I. and BLOOMBERG, S. (1975). Bifid urethra with pre-anal accessory track (Y Duplication). *British Journal of Urology*, **47**, 877-882.

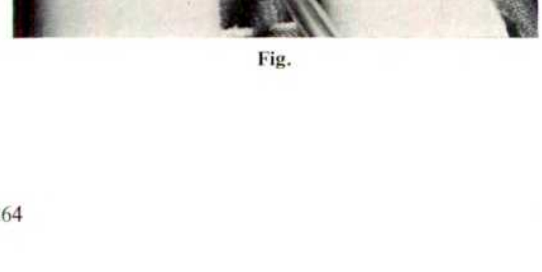


Fig.

British Journal of Urology (1976), **48**, 265–267 ©

Random Bone Marrow Biopsy in the Staging of Carcinoma of the Prostate

JOHN CRISP
Norfolk and Norwich Hospital, Norwich

Histological examination of the bone marrow is a well-established method of demonstrating the presence of metastatic tumour cells in patients with a primary cancer elsewhere. Bone marrow biopsy is a standard technique in the staging of lymphomas (Crowther and Bateman, 1972) and its use has been reported in patients with carcinoma of the prostate. Welsh and Mackinney (1964) reported 18 patients in whom 7 had positive bone marrow aspirates and in 5 of these the bone marrow results were the only evidence of disseminated disease. Mehan *et al.* (1966) reported 49 patients with proven carcinoma of the prostate, of whom 11 (22%) had positive sternal marrow aspirates and in 3 of these it was the only evidence of dissemination. Chua, Ackermann and Veenema (1969) reported on 70 patients and in 3 of the 27 with positive marrow biopsies it was the only evidence of extension of the disease beyond the prostate. Nelson, Boatman and Flocks (1973) reported on 449 patients, 33 of whom had positive marrow biopsies and 10 of these were otherwise free of detectable metastatic disease. In none of these series did the patients have bone scans, although all had X-ray skeletal surveys and serum acid phosphatase estimations.

The consensus of opinion from these series was that bone marrow estimation was of limited value in the staging of carcinoma of the prostate due to the large number of false negatives but nevertheless some patients were shown to have metastases in bone marrow when it was thought on all other clinical grounds that the disease was still confined to the prostate. The finding of metastatic cells in the marrow obviously influenced the choice of treatment and ruled out treatment such as total prostatectomy or radical radiotherapy. Bone marrow biopsy was therefore, of some value in selecting the appropriate treatment in a few patients.

Contreras, Ellis and Lee (1972) reported on positive marrow examinations in 100 patients with primary cancers in other sites. Their study clearly showed the superiority of bone marrow biopsy over bone marrow aspirates in the demonstration of metastatic tumour cells. (Biopsy was clearly positive in 94 patients, while the aspirate in only 43.)

This paper reports the results of random bone marrow biopsies in 28 patients with proven carcinoma of the prostate. The results are compared with other tests used to stage the disease, including bone scanning.

Patients and Methods

28 patients attending the Norfolk and Norwich Hospital were studied between August 1974 and August 1975; all had histologically proven carcinoma of the prostate except case No. 27, who had an occult primary with skeletal metastases. Ages ranged from 50 to 87 years. 22 were new cases and 6 were known cases of carcinoma of the prostate who required re-admission to hospital for further treatment (relief of obstruction 3, palliation of bone pain 2 and terminal nursing care 1). Clinical staging has been carried out according to the T.N.M. Protocol (Wallace, Chisholm and Hendry, 1975).

Bone marrow biopsy was performed using a Gardner-type needle under local anaesthetic from the right posterior iliac spine. These were random biopsies as no attempt was made to take the material from sites suggested by X-rays or bone scan to be involved with metastases. The bone marrow biopsies were preserved in formalin, decalcified, sectioned and stained with haematoxylin and eosin.

Table

Case No.	Age	T.N.M.	P	G	Bone biopsy	Bone scan	X-ray	Acid phosphatase
New Cases								
1	50	T_2NxM0	Px	G2	–	0	–	–
2	58	T_2NxM0	Px	G2	–	–	–	–
3	61	T_3NxM1c bone	Px	G2	+	+	+	+
4	63	T_4NxMo	Px	G3	–	–	–	0
5	64	T_2NxM1c bone	Px	G2	–	+	+	+
6	69	T_3NxM0	Px	G2	–	–	–	–
7	70	T_2NxM1b bone	Px	G2	–	+	–	–
8	72	T_3NxM1c bone	Px	G2	+	+	–	+
9	73	T_3NxM1a	Px	G2	–	–	–	+
10	74	T_2NxM1b bone	Px	G2	–	+	–	0
11	74	T_4NxM1c bone	Px	G2	+	+	–	+
12	74	T_3NxM1c bone	Px	G2	–	+	–	+
13	74	ToNxM0	Px	G2	–	–	–	0
14	75	T_2NxM1b bone	Px	G1	–	+	–	–
15	76	T_4NxM1b bone	Px	G2	–	–	+	–
16	76	T_3NxM1c bone	Px	G3	–	+	+	–
17	77	T_2NxM0	Px	G3	–	–	–	–
18	78	T_2NxM0	Px	G2	–	+	–	0
19	78	T_2NxM1b bone	Px	G3	–	+	–	–
20	85	ToNxM0	Px	G2	–	–	–	–
21	86	T_3NxM0	Px	G3	–	–	–	–
22	87	T_2NxM0	Px	G1	–	–	–	–
Old Cases								
23	59	T_2NxM1c bone	Px	G2	+	+	+	+
24	68	T_3NxM1c bone	Px	G3	+	+	+	+
25	70	T_4NxM1c bone	Px	G3	–	0	+	–
26	73	T_4NxM1c bone	Px	G3	–	+	+	0
27	74	ToNxM1c bone	Px	G0	+	0	+	+
28	82	T_4NxM0	Px	G3	–	–	–	–

– = Negative. + = Positive.
0 = Not done.

Bone scanning was done on a double-headed Ohio Nuclear Rectilinear Scanner 4 hours after injection of 8 to 10 millicuries of 99M Technesium diphosphonate.

All patients had conventional *skeletal X-ray surveys* and the majority had serum acid phosphatase estimations. All the tests were done within a short time of the bone marrow biopsy being taken. Lymphangiograms were not done on these patients.

Results

The Table summarises the results in the 28 patients studied.

Discussion

6 (28·5%) of the random bone marrow biopsies were positive but in none of these was the positive result an unexpected finding as other tests suggested that there were bony metastases present. In 2 of the 6 patients with positive bone marrow biopsies the conventional skeletal survey was negative, although in both these cases the bone scan was positive. The findings of positive mar-

row biopsies and normal X-rays have been reported previously and were mentioned in the introduction to this paper.

In 1 patient (case No. 27) the bone marrow biopsy gave the only definite histological proof of the presence of a carcinoma of the prostate. This man presented with prostatic symptoms and on clinical grounds a carcinoma was suspected. However, prostatic needle biopsies and transurethral resection specimens showed benign hyperplasia only. A year later his general condition had deteriorated, X-rays showed osteoblastic metastases in the pelvis and spine and his serum acid phosphatase was raised. Bone marrow biopsy confirmed the presence of metastases from a carcinoma of the prostate.

Accurate staging of the disease is mandatory if radical ablation of the primary tumour is being considered. It is also necessary in clinical trials evaluating or comparing different methods of treatment. The technique of bone marrow needle biopsy is a simple and painless test, free of complications, which can be performed in the ward or out-patient clinic. In addition to random bone marrow biopsies, selective biopsies can be used to obtain material for histological examination in the investigation of suspicious areas on bone scan or X-ray (Chua *et al.*, 1969).

Bone marrow biopsy, therefore, has a place in the staging of the disease and is particularly indicated when other investigations are negative in order to exclude metastatic disease with certainty.

Summary

Random bone marrow biopsies were examined in 28 patients with proven carcinoma of the prostate. In 6 cases (28·5%) bony metastases were demonstrated and in 2 of these X-ray skeletal surveys were negative.

It is suggested that bone marrow biopsy should be done in the staging of carcinoma of the prostate when other investigations are negative, especially when an occult primary is suspected, when radical treatment is contemplated and in clinical trials.

I am grateful to Mr N. A. Green and Mr M. H. Askhen for allowing me to study their patients and for their help in the preparation of this paper. I should also like to thank Dr P. Roberts for reviewing the histological sections, Dr J. Visick for reviewing the X-rays and bone scans, and Mrs S. Green and Miss L. Birch for their secretarial assistance.

References

CHUA, D. T., ACKERMANN, W. and VEENEMA, R. J. (1969). Bone marrow biopsy in patients with carcinoma of the prostate. *Journal of Urology*, **102**, 602-606.

CONTRERAS, E., ELLIS, L. D. and LEE, R. E. (1972). Value of the bone marrow biopsy in the diagnosis of metastatic carcinoma. *Cancer*, **29**, 778-783.

CROWTHER, D. and BATEMAN, C. J. J. (1972). Malignant disease. *Clinics in Haematology*, **1**, 447-473.

MEHAN, D. J. BROUN, G. O., HOOVER, B. and STOREY, G. (1966). Bone marrow findings in carcinoma of the prostate. *Journal of Urology*, **95**, 241-244.

NELSON, C. M. K., BOATMAN, D. L. and FLOCKS, R. H. (1973). Bone marrow examination in carcinoma of the prostate. *Journal of Urology*, **109**, 667-670.

WALLACE, D. M., CHISHOLM, G. D. and HENDRY, W. F. (1975). T. N. M. classification for urological tumours (U.I.C.C.)—1974. *British Journal of Urology*, **47**, 1—12.

WELSH, J. F. and MACKINNEY, C. C. (1964). Experience with aspiration biopsies of the bone marrow in the diagnosis and prognosis of carcinoma of the prostate gland. *American Journal of Clinical Pathology*, **41**, 509-512.

The Author

John Crisp, FRCS, Urological Registrar (now Senior Registrar, Department of Urology, Guy's Hospital, London SE1).

British Journal of Urology (1976), **48**, 268 ©

Short Case Report

Regression of Penile Metastases of Prostatic Carcinoma with Cyproterone Acetate Therapy

The patient, aged 58 years, had prostatic carcinoma since 1969. Originally the tumour was localised to the gland and seminal vesicles (T3); there was no elevation of the prostatic fraction of the serum acid phosphatase and there was no radiological evidence of bone deposits. The diagnosis was confirmed by histological examination of tissue resected to relieve outflow obstruction. In June 1974 he presented with metastases in the corpora cavernosa, producing painful priapism (Fig.). This caused obstruction by urethral compression; the urethra would not admit a 6F catheter. From 1969 he had been regularly taking Premarin, 2·5 mg t.d.s. with effective lowering of the plasma testosterone, the serum acid phosphatase remaining normal throughout. Until developing the penile metastases he had been well and symptom free. He was treated by intravenous Honvan without effect on the priapism; local external irradiation failed also. He developed urinary retention with overflow and permanent suprapubic cystostomy was considered. However, he was given cyproterone acetate, 100 mg t.d.s.: within 2 days the rock-hard penile deposit, originally 2 × 5 cm in size, had softened and he could void with a flow rate of 2 ml/min; after 7 days the priapism disappeared and the flow rate was 5 ml/min. The present flow rate is 15 ml/min. Now he is symptom free and the metastasis can be felt only as a soft lesion 0·5 cm in size. There is no evidence of metastases elsewhere. The serum testosterone levels are as follows: Pre-treatment levels not available in 1969; 1972 while on Premarin, 100 nG/100 ml; after intravenous Honvan, 100 nG/100 ml; following cyproterone acetate 50 nG/100 ml. The patient had not been castrated or treated with pituitary irradiation.

Comment

Genital metastases of prostatic cancer are uncommon (Iverson and Blackard, 1972.) In this case it produced outflow obstruction: conventional hormonal therapy failed and external irradiation had no effect. Cyproterone acetate, an anti-androgen used to treat male sexual deviants, has been used to treat prostatic cancer with encouraging results (Geller *et al.*, 1968; Smith *et al.*, 1973). Currently the use of cyproterone acetate in prostatic cancer is being evaluated. It lowers the serum acid phosphatase and plasma testosterone and may prove of value in the treatment of oestrogen insensitive prostatic carcinoma.

This paper was presented to the Section of Urology, Royal Society of Medicine who have given consent for publication.

R. M. JAMESON
Liverpool Regional Urological Centre, Sefton General Hospital, Liverpool 15

References

GELLER, J. VAZAKAS, G., FRUCHTMAN, B., NEWMAN, H., NAKAO, K. and LOH, A. (1968). The effect of cyproterone acetate on advanced carcinoma of the prostate. *Surgery, Gynecology and Obstetrics*, **127**, 748-758.

IVERSON, A. P. and BLACKARD, C. E. (1972). Carcinoma of the prostate with urethral metastases. *Journal of Urology*, **108**, 901-904.

SMITH, R. B., WALSH, P. C. and GOODWIN, W. E. (1973). Cyproterone acetate in the treatment of advanced carcinoma of the prostate. *Journal of Urology*, **110**, 106-108.

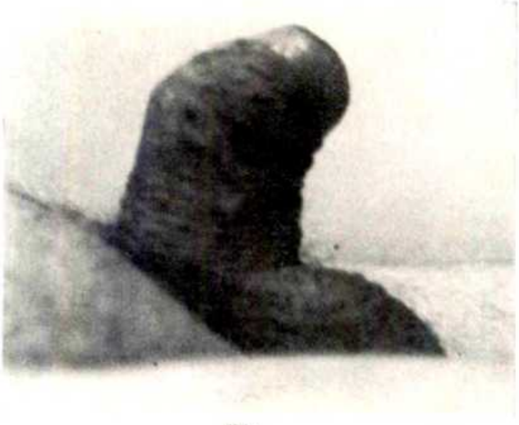


Fig.

British Journal of Urology (1976), **48**, 269-273 ©

Amoebiasis of the Penis

JOHN A. THOMAS and A. JOSEPH ANTONY

Departments of Pathology and Surgery, St. John's Medical College, Bangalore, India

Amoebic infections of the penis are extremely rare and are usually mistaken clinically for a cancer or an ulcerative venereal disease. On reviewing the world literature, it was found that only 8 such cases have been reported in the last 51 years (Shih, Wu and Lieu, 1939; Hermann and Berman, 1942; Camecho and Beirana, 1959; Mylius and Ten Seldam, 1962; Talwalkar, 1962; Quevedo and Elias Dib, 1963; Purpon, Jiminez and Engelking, 1967). To this small number one more case has been added. Comparisons between the case presented here and those reported in the world literature have been made.

Case Report

A 35-year-old Indian male came to the Surgical Outpatient Clinic with a 1-month history of a rapidly growing painful penile swelling that had ulcerated. This swelling was associated with burning on micturition of 3 weeks' duration. The patient denied any history of extramarital venereal contacts or of homosexual practices.

Physical examination, revealed the patient to be in acute distress with a large circumferential irregular ulceration of the penis which involved the entire glans and extended dorsally, to involve the distal two-thirds of the shaft and ventrally, extended up to the penoscrotal junction. The margins of the ulcer in some areas were everted. The base of the ulcer was covered with serosanguinous, necrotic material and part of the glans and shaft of the penis appeared to be infiltrated. The whole lesion was acutely tender and bled easily (Fig. 1). The superficial horizontal group of inguinal lymph nodes were bilaterally enlarged, firm, non-tender and mobile.

A provisional diagnosis of *Lymphogranuloma Venereum* was made and a biopsy done.

The specimen received consisted of a wrinkled 2 cm piece of pigmented excoriated skin, beneath which a large amount of grey-brown necrotic "shaggy" debris was noted.

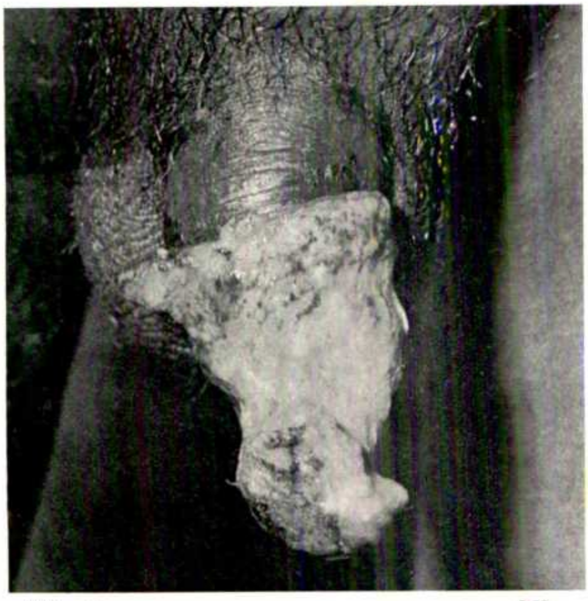


Fig. 1. Amoebiasis of the penis. Note the gross ulceration of the glans and shaft of the penis which could be easily mistaken for an ulcerative carcinoma.

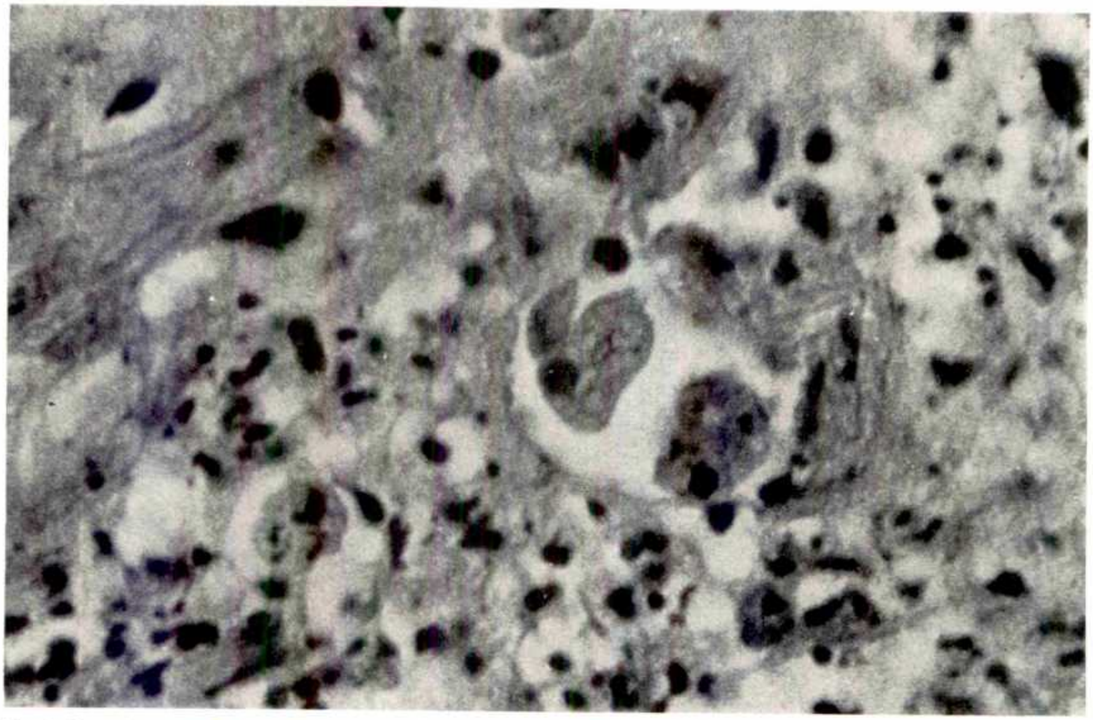
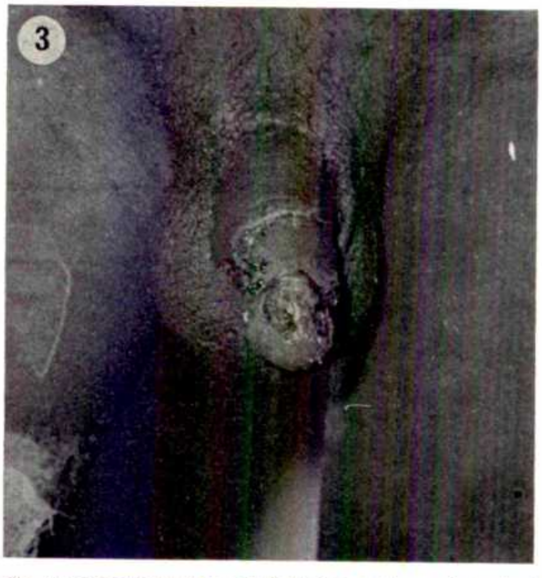


Fig. 2. Note the trophozoite forms of *Entamoeba histolytica* within thin-walled vascular channels. The pale coloured vacuoles within the organisms are ingested red cells. Haematoxylin-eosin × 1,200.



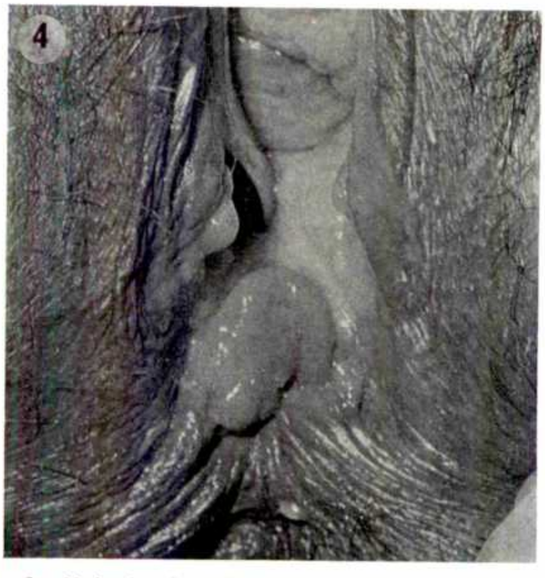


Fig. 3. Complete healing of the lesion on the penis took place after 10 days' antiamoebic therapy. A skin graft was subsequently done from the right anterior thigh.

Fig. 4. The 28-year-old spouse of the above patient had a 1 cm granuloma at the vaginal orifice.

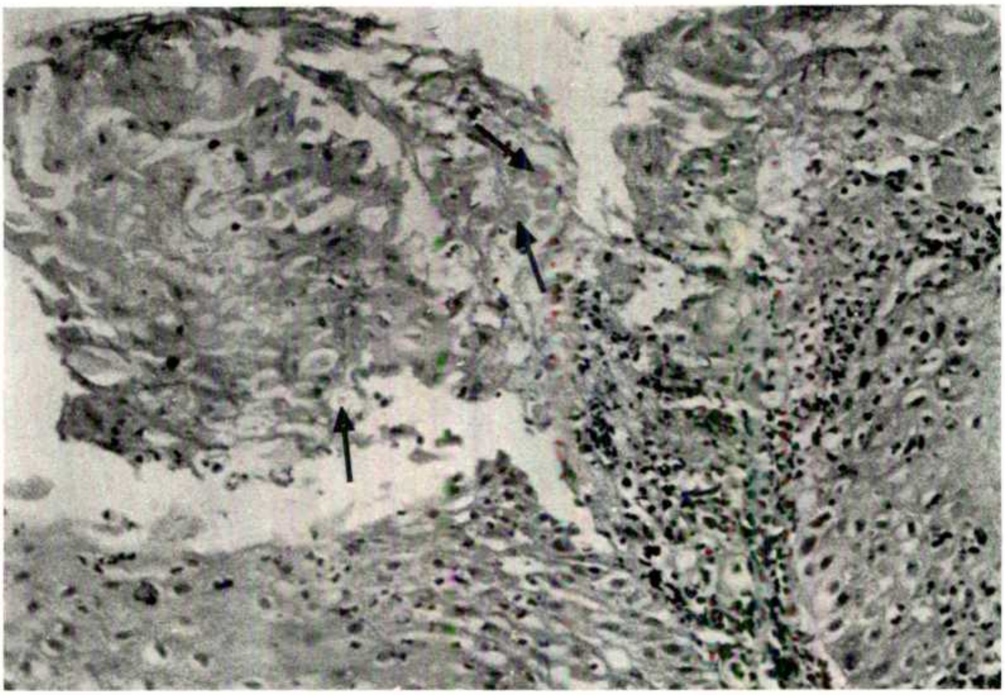


Fig. 5. Note the superficial mucosal ulceration of the vagina with clusters of *Entamoeba histolytica* in the necrosed epithelium. Haematoxylin-eosin. × 35.

Histologically, beneath a strip of skin many abscesses were seen with some evidence of granulation tissue formation. Much necrotic blue-pink debris was noted intermixed with which, numerous trophozoite forms of *Entamoeba histolytica* were seen, measuring between 20 microns and 40 microns. These trophozoite forms contained ingested red blood cells. The iron-haematoxylin stain showed the typical nuclear structure of this species of amoeba—a central karyosome and chromatin aggregates situated peripherally near the nuclear membrane. Occasional trophozoite forms were seen within thin-walled vascular channels (Fig. 2). A histopathological diagnosis of a "Chronic inflammation of the penis caused by organisms morphologically similar to trophozoite forms of *Entamoeba histolytica*" was made.

Treatment was instituted with emetine hydrochloride (60 mg per day for 10 days) and metronidazole (600 mg per day for 10 days) and the lesion healed rapidly within a period of 10 days. Since much destruction of the penile shaft had taken place, a skin graft from the right thigh on to the penis was done, which took perfectly (Fig. 3).

None of the investigations, including urinary sediment examination and fresh preparations of the exudate taken from the ulcer on the penis, was positive for amoeba.

In order to determine the source of his infection, the patient was repeatedly questioned and revealed that his wife had had "diarrhoea with blood and mucous", sometime previously. She was 28 years old and was brought in for clinical examination. This examination revealed that she had leucorrhoea due to a chronic vaginitis. Many small reddish-coloured ulcers were seen, on the vaginal mucosa. At the vaginal orifice a 1 cm red granuloma was seen (Fig. 4). The vaginal pH was altered and alkaline.

As fresh preparations proved negative for amoeba a biopsy of 1 of these vaginal ulcers, was done and showed areas of ulceration of the squamous epithelium in which were seen clusters of organisms morphologically similar to *Entamoeba histolytica* (Fig. 5).

Treatment consisted of emetine hydrochloride (60 mg per day for 10 days) and metronidazole (600 mg per day for 10 days). Good results were obtained.

Discussion

It is obvious from a study of the Table that penile amoebiasis has affected individuals of many age-groups. The youngest individual was 25 years old and the oldest 65 years. The chief complaint

Table

Amoebiasis of the Penis

Authors	Source of report/ nationality of patient	Age of patient (in years)	Complaint	Duration (in months)	Antecedent causes	Inguinal lymph node status	Mode of diagnosis
1. Straub (1924) (Ref. Talwalkar)	Chinese	—	—	—	Coitus per anum	NM	—
2. Shih, Wu and Lieu (1939)	China	54	Pain, swelling ulceration	—	Phimosis (spouse not examined)	Palpable Not tender Not fixed	Biopsy positive Fresh preparations: positive
3. Hermann and Berman (1942)	USA	25	Pain, ulcer	6	History of amoebic dysentery and venereal contact	NM	Biopsy negative Fresh preparations: positive
4. Camacho and Beirana (1959)	Mexico	25	Pain, itching	3	Pederasty	Palpable	Biopsy negative Culture of secretion: positive
5. Mylius and Ten Seldam (1962)	New Guinea	47	Ulcer	1	Phimosis (spouse with amoebic vaginitis)	Not palpable	Biopsy positive
6. Talwalkar (1962)	India	65	Pain, ulcer	6	No history of dysentery (spouse not infected) No history of homosexuality	NM	Biopsy positive Fresh preparation: positive
7. Quevedo and Elias Dib (1963)	Mexico	65	Dysuria	5	Phimosis	Palpable	Biopsy positive
8. Purpon, Jiminez and Engelking (1967)	Mexico	31	Pain Burning sensation	22/30	Homosexual relations	NM	Biopsy positive
9. Present authors (1975)	Indian	35	Pain, ulcer	1	Spouse with amoebic vaginitis	Discrete, painless	Biopsy positive Smear negative

NM: Not mentioned. Positive: For *E. histolytica*.

of 6 of the patients was pain with ulceration, the ulcers having appeared gradually and spread over the entire glans and shaft of the penis over a period of 22 days to 6 months. The symptom of pain appears to be important in differentiating this ulcerative chronic inflammation from a cancer; Thomas and Small (1968) in a retrospective study of penile carcinomas from Southern India, found that their patients had complained of ulceration, penile growth, phimosis and dysuria with discharge but none had complained of pain.

In tracing the pathogenesis of the lesion, it is significant that 3 of 4 patients below the age of 40 years had a history of homosexuality and venereal contact, while those over that age either had a phimosis or apparently did not practise adequate sex hygiene. Phillips *et al.* (1955) proved experimentally that the responsibility for the production of an amoebic lesion rested not only on the amoebae but also on their microbial associates; in the absence of these microbial associates the amoebae appeared harmless.

The diagnosis of penile amoebiasis, has been established by means of a biopsy in 6 of the 8 reported patients. Fresh preparations and culture have been used to good advantage, but only after the biopsy suggested the diagnosis.

Summary

The 9th patient in world literature with penile amoebiasis, is reported.

An extensive review of world literature suggests that the main diagnostic symptomatology in penile amoebiasis is pain with ulceration, in contrast to ulcerative carcinomas of the penis, which are painless.

The possible antecedent causes could be homosexuality, venereal contacts, phimosis with resultant inadequate sex hygiene.

The authors wish to thank Dr C. M. Francis, MB, BS, PhD, Dean of this College for permission to make this report. The secretarial assistance of Mrs L. A. Menon is acknowledged.

References

CAMACHO, B. S. and BEIRANA, L. (1959). Amibiasis cutanea genital. *Dermatologia*, **3**, 127-133.

HERMANN, H. B. and BERMAN, L. S. (1942). Penile ulcer caused by *Endameba histolytica*. *Journal of the American Medical Association*, **120**, 827-828.

MYLIUS, R. E. and TEN SELDAM, R. E. (1962). Venereal infection by *Entamoeba histolytica* in a New Guinea native couple. *Tropical and Geographical Medicine*, **14**, 20-26.

PHILLIPS, B. P., WOLFE, P. A., REES, C. W., GORDON, H. A., WRIGHT, W. H. and REYNIERS, J. A. (1955). Studies on the ameba-bacteria relationship in amebiasis. *American Journal of Tropical Medicine and Hygiene*, **4**, 675-692.

PURPON, I., JIMENEZ, D. and ENGELKING, R. L. (1967). Amebiasis of the penis. *Journal of Urology*, **98**, 372-374.

QUEVEDO, A. M. and DIB, J. ELIAS (1963). Un caso de amibiasis del pene. *Medicina*, **43**, 240-243.

SHIH, H. E., WU, Y. K. and LIEU, V. T. (1939). Amoebiasis of the penis. *Chinese Medical Journal*, **55**, 139-145.

TALWALKAR, G. V. (1962). Amoebiasis of the penis. *Journal of the Indian Medical Association*, **39**, 103-104.

THOMAS, J. A. and SMALL, C. S. (1968). Carcinoma of the penis in Southern India. *Journal of Urology*, **100**, 520-526.

The Authors

John A. Thomas, MD, Professor and Head of Pathology.
A. Joseph Antony, FRCS, FICS, FAAS, Assistant Professor of Surgery.

Requests for reprints to Dr John A. Thomas, Professor and Head, Department of Pathology, St. John's Medical College, Bangalore-560034, India.

British Journal of Urology (1976), **48**, 274 ©

Short Case Report

Tuberculosis of the Penis

Tuberculosis of the penis is a rare clinical manifestation of the disease. Genito-urinary tuberculosis is still seen in Europe but the penile lesion is very uncommon. In 1878, Fournier (cited by Lewis) described the first case of primary tuberculosis of the penis. Since then very few cases have been reported. This present case is being presented because of the extreme rarity of the disease and to draw attention to this entity.

Case Report

R. D., A 66-year-old unmarried farmer, was admitted to St Vincent's Hospital, Dublin with a painless ulcer on the glans penis of 4 months' duration. No history of trauma. On examination a small irregular ulcer with granulation tissue covering the floor was seen on the glans penis. It was tender to touch and indurated. Scrotum and testes were normal. The ulcer did not look like early carcinoma. Chest X-ray normal. No previous history of tuberculosis. Serogical tests for syphilis were negative. Intravenous pyelogram was normal. Excision biopsy of the ulcer was performed. Histology proved it to be tuberculous ulcer of the glans penis (Fig.). Patient was treated with antituberculous drugs following which the ulcer healed completely. The patient was followed up for 2 years.

Comments

Tuberculosis of the penis is rare (Kaufman and Silver, 1954) whereas tuberculosis of the epididymis and testes is much more common. The diagnosis can only be made by histology and treatment with antituberculous drugs is curative. Tuberculous disease of the penis may be of primary or secondary type, depending upon the absence or presence of co-existing tuberculous disease elsewhere in the body. In the present case there was no focus in the lungs and none could be demonstrated in the genito-urinary tract.

A. Sriman Narayana, D. G. Kelly and F. A. Duff
Dept. of Urology, St Vincent's Hospital, Elm Park, Dublin 4

Reference

Kaufman, J. J. and Silver B. B. (1954). Tuberculous ulcer of the penis: primary surgical excision. *Journal of Urology*, **72**, 226-229.

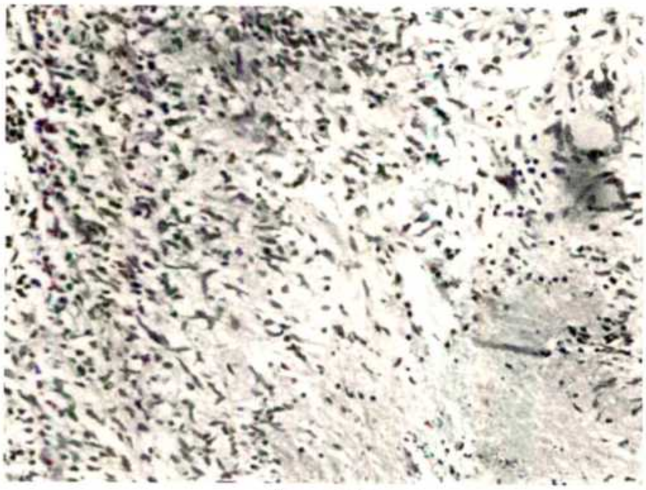


Fig. (× 125)

British Journal of Urology (1976), 48, 275–277 ©

Vasoplasty: a New Technique

V. R. NAIR
General Hospital, Trivandrum, India

Vasoplasty methods are tedious, time consuming and generally associated with a high rate of failure. In countries where vasectomy is widely used as a method of sterilisation it is inevitable that some of these cases will require surgical reversal. Some centres are now using the operating microscope for this operation; the technique to be described is simple and does not call for complicated and costly equipment.

Indications

In India, vasectomy is the commonest method of male sterilisation. Thousands of young men with one or more children undergo this operation so that methods for screening the candidates tend to be inadequate. Hence, although the main indications are the loss of children due to accidents or illness and divorce and remarriage (Table I), one of the indications for reversal may be psychological.

Patients

During a 5-year period from 1967 to 1971, a personal series of 28 cases was carried out, of which 14 were done in 1971 alone. The age of the patients ranged from 19 to 50; 15 were in the 21 to 30 age group while none was over 50. The time since the vasectomy ranged from less than 1 year to over 5 years (Table II).

Technique

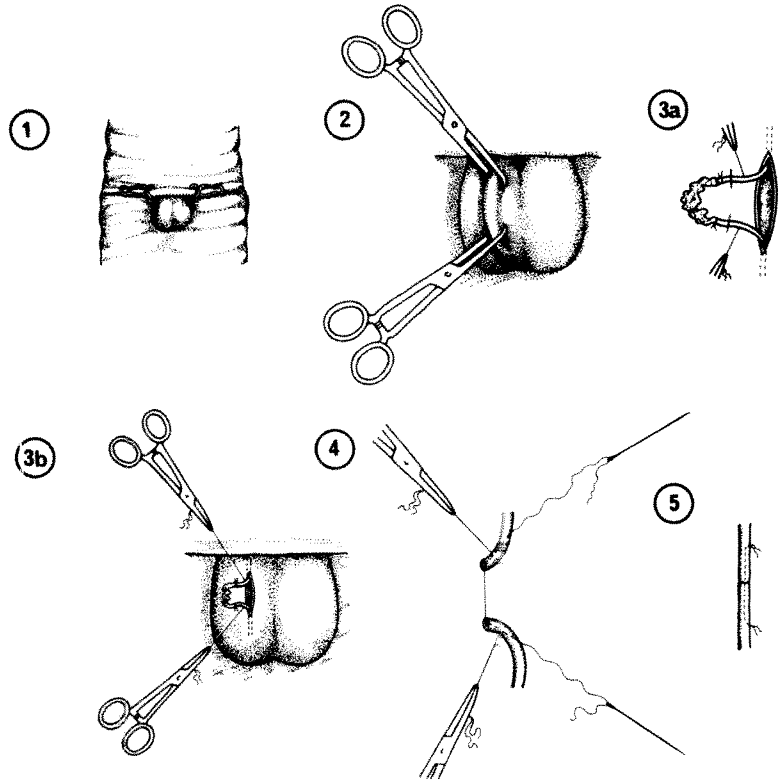
All of the patients had had a semen analysis to confirm azoospermia. Spinal anaesthesia was used except when contra-indicated. Local anaesthesia was not used in this series. The patient was placed in the supine position and the scrotum prepared and draped (Fig. 1). The stumps of the vasa were palpated and steadied with a pair of tissue forceps (Fig. 2). An incision about 4 cm was made through the skin and subcutaneous tissue and by blunt and sharp dissection, the stumps were mobilised and identified. It was noted that a strand of fibrous tissue always connected the two stumps (Fig. 3). The stumps were then held by stay sutures and the ends pared carefully

Table I

Indications	No. of cases
Psychological	1
Death of children	14
Divorce and remarriage	10
Others	3
Total	28

Table II

Duration of vasectomy	Less than 1 year	Less than 2 years	Less than 3 years	Over 5 years
No. of cases	2	6	12	8
Total	28 cases			



Figs. 1-5. Showing each step in vasoplasty.

using a sharp knife until the lumen of the vas was clearly visible (Fig.3a). A piece of 3/0 plain catgut with an intestinal needle on each end was threaded into the lumen of the vas and brought out of the sides (Fig. 4). The catgut acts as a splint around which the ends of the vas remain in apposition. Knots were tied at either end to ensure continued apposition (Fig. 5). Complete haemostasis was obtained. The wound was closed in one layer with interrupted silk.

Follow-up and results

The patients stayed in hospital until the skin sutures were removed on the 7th day. Complete bed rest was not insisted upon; all vasoplasty patients were on prophylactic antibiotic therapy. After discharge from hospital, they were seen at 3 and 6 weeks. If the semen analysis on two occasions did not show motile spermatozoa, the operation was considered a failure; a repeat operation was advised after 6 to 10 months. It was not possible to follow-up the patients to determine the incidence of pregnancy.

A direct relation between the duration of vasectomy and success with recanalisation was noted. All the cases which failed belonged to the over 5-year vasectomy group. 1 patient was operated upon 8 years after the vasectomy. Thus, the longer the duration, the less the chances for a successful recanalisation.

All 28 cases showed preoperative azoospermia and only 4 showed postoperative azoospermia—a failure rate of 16·6%. Details of the follow-up semen analysis at 6 weeks are shown in Table III.

Table III
Semenalysis 6 Weeks after Operation

	Over 40 million per ml	Over 30 million per ml	Over 20 million per ml	Less than 20 million per ml	Total No. of cases
No. of cases	7	10	5	2	24
Motility	40% motile	30% motile	25% motile	20% motile	Total No. of cases
No. of cases	8	10	3	3	24

Discussion

It was possible to halve the operating time to 45 min for a bilateral procedure, as further experience with this operation was obtained. Complete haemostasis and the absence of sepsis contributed to a successful result. Paring the stumps until a healthy lumen was visualised, gentle handling and minimal devitalisation of tissues were also important factors.

A short stump at the proximal end of the vas would make this operation more difficult. It has been advised that at the time of vasectomy, as far as possible, a stump of 3·5 to 4 cm should be ensured. The routine use of non-absorbable material at the time of a vasectomy helps in subsequent identification of the stumps; it also prevents spontaneous recanalisation of the vas (Marshall and Lyon, 1972).

Splinting the vas both externally and internally has been studied in experimental animals (Moon and Bunge, 1967). A technique with lateral reanastomosis over a nylon splint was successful in 17 out of 19 cases (Mehta and Ramani, 1970). Internal splinting with absorbable material as used in this series has been similarly successful.

It is hoped that the simplicity of this operation will appeal to doctors working in smaller hospitals.

Summary

A technique by which plain catgut is used as an internal splint in vasoplasty is described.

28 cases have been carried out, of which only 4 have failed.

I wish to thank the Director of Health Services, Kerala, India for permission to publish; Dr Eugene T. Dmytryk, Surgeon at St John's Hospital, St Louis, M.O., USA, from whom I first came to know of this technique; Johnson and John (India) Ltd., for manufacturing and supplying free of cost, plain catgut with eyeless needles at both ends which were used in the later series; and the Superintendent and staff of General Hospital Trivandrum, where all the operations were done.

References

MARSHALL, S. and LYON, R. P. (1972). Transient reappearance of sperm after vasectomy. *Journal of the American Medical Association*, **219**, 1753-1754.

MEHTA, K. C. and RAMANI, P. S. (1970). A simple technique of re-anastomosis after vasectomy. *British Journal of Urology*, **42**, 340-343.

MOON, K. H. and BUNGE, R. G. (1967). Splinted and nonsplinted vasovasostomy: experimental study. *Investigative Urology*, **5**, 155-160.

The Author

V. R. Nair, FRCSE, Surgeon (now Surgical Specialist, Kitwe Central Hospital, P.O. Box 969, Kitwe, Zambia).

British Journal of Urology (1976), **48**, 278 ©

Short Case Report

Congenital Urethral Polyp in a Child

A 5-year-old boy presented with haematuria and urinary retention. Investigation of similar complaints at age 1 year had been normal, although a micturating cystourethrogram was incomplete as the child would not void. On this admission, urine culture was sterile and IVP showed blunting of the superior calyces. Micturating cystourethrography showed a large polyp arising from the verumontanum on a thin stalk (Fig. 1). There was no evidence of vesicoureteric reflux. Cystoscopy confirmed the polyp and transvesical excision was performed (Fig. 2). Histological examination showed the polyp to have a fibrovascular core covered with stratified squamous epithelium.

Comment

Urethral polyps in children occur exclusively in boys; the average age is 5·2 years. While Stephens (1963) found 5 cases in 75 investigations, the usual incidence is much lower and only 31 cases have been reported. Micturating cystourethrography is diagnostic. Vesicoureteric reflux is reported in 3 of 4 cases by Williams (1968) but is not mentioned in Stephens' series. Transvesical excision is most commonly employed although transurethral excision may be used in older children. The polyps are usually covered by transitional epithelium and while squamous metaplasia has been noted this case would appear to be the first with stratified squamous epithelium. Although the aetiology is unknown, Downs (1970) has suggested the most appropriate designation is congenital polyp of the urethra.

F. H. Bagley and A. I. Davidson
Royal Aberdeen Children's Hospital.

References

Downs, R. A. (1970). Congenital polyps of the prostatic urethra. *British Journal of Urology*, **42**, 76-85.

Stephens, F. D. (1963). *Congenital Malformations of Rectum, Anus and Genitourinary Tract*. Philadelphia: Saunders, p. 231.

Williams, D. I. (1968). *Paediatric Urology*. London: Butterworths, p. 263.

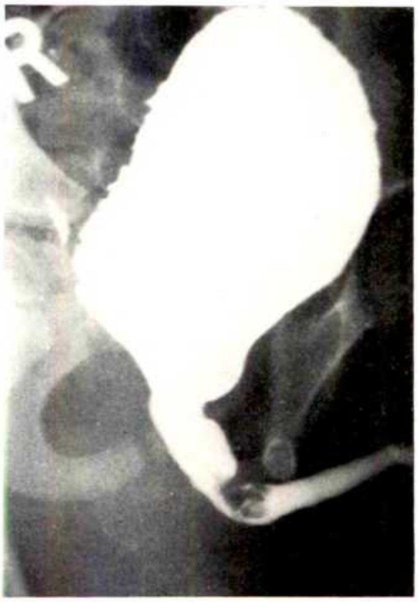


Fig. 1. Micturating cystourethrogram showing polyp on a slender stalk arising from posterior urethra.

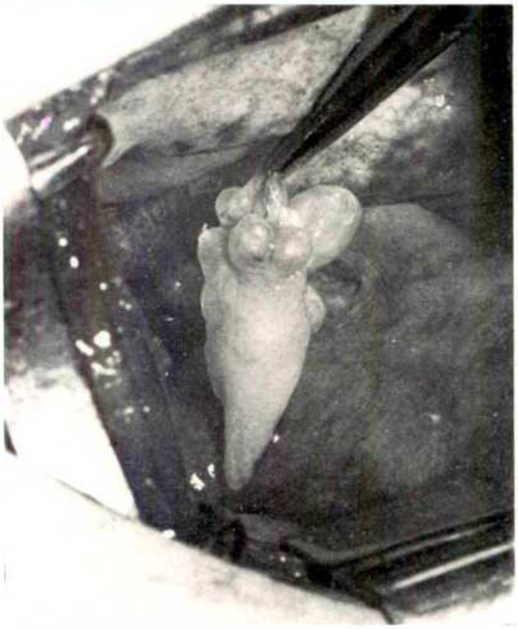


Fig. 2. Polyp as it appeared through the bladder.

British Journal of Urology (1976), **48**, 279-283 ©

Comparison of Sterile Bag, Clean Catch and Suprapubic Aspiration in the Diagnosis of Urinary Infection in Early Childhood

J. D. HARDY, P. M. FURNELL and W. BRUMFITT

Department of Paediatrics and the Department of Medical Microbiology, The Royal Free Hospital, London

Mistakes in the diagnosis of urinary tract infection are common because of the well-known difficulty in distinguishing between genuine bacteriuria and contamination.

This problem has been critically reviewed by Norden and Kass (1968). Wrong diagnosis may have far-reaching consequences, particularly in children, since a false positive result may lead to unnecessary urological investigation and treatment of a non-existent urinary infection. Alternatively, a false negative result may mean that neither investigation nor treatment is carried out so that renal damage which could have been prevented may occur. Radiological abnormalities may be detected in up to 50% of infants and children presenting with infection of the urinary tract (Smellie *et al.*, 1964). Because of the high yield of urinary tract abnormalities found, urological investigation is indicated after the first diagnosed infection in both sexes (Kunin *et al.*, 1962). It is therefore very important to make the right diagnosis and this makes accurate examination for infection essential.

Methods commonly used in paediatric practice for urine collection are the bag, clean catch and suprapubic aspiration. Reports comparing the results of 2 of the above are: bag and clean catch (Boehm and Haynes, 1966); suprapubic and clean catch (Bergwall and Ljungblom, 1972); suprapubic and bag (Newman, O'Neill and Parker, 1967; Bergwall and Ljungblom, 1972), and suprapubic and "clean voided" (Saccharow and Pryles, 1969; Lykken and Grögaard, 1972; Aronson, Gustafson and Svenningsen, 1973).

The term "clean voided" has been used to describe both bag and clean catch specimens. This is unfortunate because it does not permit a precise comparison of the 2 methods. In view of this we decided it would be worthwhile to carry out a direct comparison of all 3 methods to decide which is best for the detection of urinary infection.

Patients and Methods

Bag, clean catch and suprapubic specimens were obtained from 30 infants and children aged from 1 day to 3 years. 20 were male and 10 female and none had voluntary control of micturition at the time the specimens were taken. All were in-patients at The Royal Free Hospital during this study.

The perineum and suprapubic regions were cleansed with sterile swabs moistened with distilled water before collecting the specimens. The bags used were U-bags (Hollister, Chicago, USA). Clean catch specimens were collected during spontaneous micturition. Suprapubic aspiration was performed by the method described by Pryles *et al.* (1959).

All admissions to the children's ward are screened for urinary infections, the bag technique being used for those without bladder control. If bacterial growth was obtained from this first bag specimen, the child was entered into the formal study. Also entered were patients whose condition demanded immediate antimicrobial therapy where delay caused by screening could not be justified. In the latter group all 3 specimens were taken without prior screening.

The commonest complaints were neonatal jaundice, poor feeding, poor weight gain, vomiting, diarrhoea, fever and febrile convulsions. All these conditions may be associated with urinary tract infection.

Table I

Microscopy and Microbiology of Urine Specimens from 30 Infants and Children

			Bag specimen*			Clean catch specimen*			Suprapubic specimen*		
Case No.	Sex	Age	WBC (mm^3)	Bacteria (per ml)	Culture	WBC (mm^3)	Bacteria (per ml)	Culture	WBC (mm^3)	Bacteria (per ml)	Culture
1	M	2 dy	100	NG	...	>100	NG	...	0	NG	...
2	M	3 dy	0	$>10^5$	Mixed	0	$<10^2$	Mixed	0	NG	...
3	M	6 dy	<2	10^5	Mixed	<2	10^5	Mixed	0	NG	...
4	M	7 dy	0	10^4	Mixed	0	10^4	Mixed	0	NG	...
5	F	7 dy	0	10^4	Mixed	0	10^4	Mixed	0	NG	...
6	F	7 dy	1	10^4	Mixed	1	10^4	Mixed	0	NG	...
7	M	8 dy	<2	$>10^5$	Mixed	<2	10^3	Mixed	<2	NG	...
8	F	9 dy	<2	10^5	Mixed	<2	10^4	Mixed	<2	NG	...
9	M	10 dy	2	10^4	Mixed	0	10^4	Mixed	2	NG	...
10	F	10 dy	2	10^5	Mixed	0	10^4	Mixed	0	NG	...
11	M	10 dy	200	$>10^5$	*S. aureus*	>20	$>10^5$	*S. aureus*	>100	$>10^5$	*S. aureus*
				10^4	*E. coli*		10^4	*E. coli*			
12	M	11 dy	0	NG	...	0	NG	...	0	NG	...
13	M	11 dy	1	$>10^5$	Mixed	<1	10^3	Mixed	0	NG	...
14	M	2 wk	0	$>10^5$	Mixed	0	10^4	Mixed	0	NG	...
15	M	2½ wk	0	$<10^4$	Mixed	0	10^4	Mixed	0	NG	...
16	F	1 mth	0	10^5	Mixed	0	10^5	Mixed	0	NG	...
17	M	1 mth	0	10^5	Mixed	0	NG	...	0	NG	...
18	F	1 mth	0	10^4	Mixed	<2	10^4	Mixed	0	NG	...
19	M	2 mth	0	10^5	Mixed	0	10^4	Mixed	0	NG	...
20	M	2 mth	0	10^5	Mixed	0	10^4	Mixed	0	NG	...
21	M	2½ mth	1	$>10^5$	*E. coli*	0	$<10^4$	*E. coli*	0	NG	...
22	F	3 mth	0	$>10^5$	*E. coli*	0	$>10^5$	*E. coli*	0	NG	...
23	M	3 mth	1	NG	...	<1	10^3	Mixed	0	NG	...
24	M	6 mth	0	$>10^5$	Mixed	0	10^3	Mixed	0	NG	...
25	M	6 mth	0	10^5	Mixed	0	10^3	Mixed	0	NG	...
26	F	6 mth	0	$>10^5$	Mixed	0	$<10^2$	Mixed	0	NG	...
27	M	8 mth	3	10^5	*E. coli*	2	10^4	*E. coli*	2-3	10^5	*E. coli*
28	F	15 mth	0	10^4	Mixed	>50	$>10^5$	*Proteus mirabilis*	>100	$>10^5$	*Proteus mirabilis*
							$<10^2$	*E. coli*			
29	F	16 mth	0	$>10^5$	*E. coli*	0	$>10^5$	*E. coli*	<2	$>10^5$	*E. coli*
30	M	3 yr	2	NG	...	1	NG	...	0	NG	...

NG = No growth.
* See text for details of specimen collection.

The 3 specimens (bag, clean catch and suprapubic puncture) were collected within 1 to 6 hours of each other but not always in the same order. Individual specimens were collected in sterile plastic bottles and transported to the laboratory immediately or stored at 4°C and delivered later that day.

Bacteria were quantitated on cystine lactose electrolyte deficient (CLED) culture media and read after 18 hours' incubation. The white cells were counted on unstained, uncentrifuged urine.

Results

The results of microscopy, culture and colony counts on the urine specimens are shown in Table I and a comparison of colony count results by the 3 methods of collection in Table II.

Table II

Number of Specimens with Mixed Growth, Pure Growth and no Growth from the 3 Methods of Collection

	Mixed growth	Pure growth $\geqslant 10^5$ (organisms/ml)	Pure growth $< 10^5$ (organisms/ml)	No growth
Bag	22	4 (2)*	0	4 (4)*
Clean catch	22	2 (1)*	2 (0)*	4 (4)*
Suprapubic aspiration	0	4	0	26

* Numbers in parentheses indicate number of specimens which agree with corresponding suprapubic aspiration results.

Suprapubic Aspiration Specimens. There was no growth from 26 and a pure growth of 10^5 or more organisms per ml from the remaining 4. We assumed that only these 4 had significant bacteriuria.

Bag and Clean Catch Specimens. In contrast, a feature of the results from bag and clean catch specimens was the very high incidence (73%) of mixed growth. In every case but 2 (patients 11 and 28) the mixed growth occurred from specimens that were sterile when taken by the suprapubic technique. Thus this growth must be taken to be due to contamination.

Agreement between bag, clean catch and suprapubic specimens was found in only 3 cases with no growth and 1 case with significant bacteriuria. The corresponding figures for agreement between bag and suprapubic specimens were 4 and 2 and between clean catch and suprapubic specimens 4 and 1 (Table II).

It was evident that from the 26 specimens sterile by the suprapubic technique a higher number of organisms were grown from bag specimens than from clean catch specimens, suggesting a higher contamination rate in the former. The colony count was higher in the bag than the clean catch specimen in 13, the same in 11 and lower in only 2. A *t*-test of differences between paired counts on a logarithmic scale showed a significantly higher average count by bag than by clean catch specimen ($P < 0{\cdot}005$).

Contamination of the bag and clean catch specimens was a problem in 2 of the 4 cases with significant infection.

In this series the presence or absence of pyuria was of only limited help in confirming or refuting the diagnosis of urinary tract infection (Table I).

Discussion

Bacteriuria is known to disappear spontaneously in a varying proportion of patients including infants (Littlewood, 1972). For this reason, for comparison of cultures using different methods, specimens must be collected at the shortest possible intervals (Pryles, 1965). Therefore all our collections from individual cases were taken on the same day. Some reports comparing "clean voided" specimens with suprapubic aspiration make no distinctions between the conclusions that can be drawn from bag and clean catch specimens (Saccharow and Pryles, 1969; Lykken and Grögaard, 1972; Aronson *et al.* 1973). We have been able to compare these with each other and with suprapubic aspiration specimens, the techniques of which eliminate the risk of contamination.

Distilled water was used for cleansing because of the antibacterial action of agents like chlorhexidine which can cause residual contamination of the urine and give rise to falsely low counts (Roberts, Robinson and Beard, 1967).

The widely accepted criterion for the diagnosis of urinary infection is 10^5 or more organisms/ml in pure culture. By comparison with suprapubic aspiration results it can be seen that the wrong diagnosis could be made from 4 bag results (cases 11, 21, 22 and 28) and 4 clean catch results (cases 11, 22, 27 and 28) (Table I). Although the figure for misdiagnosis (4) is small, in actual terms, it should be remembered that there were only 4 genuine infections in this series.

Unlike Smellie *et al.* (1967) we did not find bag specimens satisfactory, although in her clinic where special facilities are available it is possible to obtain good results by this method, provided that 2 consecutive specimens are cultured (Smellie and Normand, 1975). Our findings showed that even in a paediatric ward clean catch and bag specimens were unreliable. However, we agree with Boehm and Haynes' findings (1966) that clean catch specimens are more satisfactory than bag specimens although still often misleading (Table I).

Lincoln and Winberg (1964) found greater contamination from young male infants. Aronson *et al.* (1973) found greater contamination from young female infants. In this study we were unable to detect a difference between the sexes.

Conclusion

A clear difference in culture results from the 3 methods of collection could be shown. The conclusion from our findings is that doctors should be encouraged to perform suprapubic aspiration in this age group. Accurate diagnosis of urinary infection at this age is vital for proper treatment. A positive finding allows the correct management, and avoids the danger of placing the label of urinary infection on a child who has no infection.

Summary

Bag, clean catch and suprapubic specimens of urine were taken on the same day in a group of 30 unwell infants and young children.

On microbiological grounds suprapubic aspiration was far superior to clean catch collection and clean catch collection superior to bag collection in the diagnosis of urinary tract infection.

We wish to thank Dr J. M. T. Hamilton-Miller of the Medical Microbiology Department for his help; also Mrs Hillary H. Tillett of the Central Public Health Laboratories for statistical analysis.

References

Aronson, A. S., Gustafson, B. and Svenningsen, N. W. (1973). Combined suprapubic aspiration and clean-voided urine examination in infants and children. *Acta Paediatrica Scandinavica*, **62**, 396-400.

Bergwall, B. and Ljungblom, B. A. (1972). Suprapubic aspiration of the urinary bladder for accurate diagnosis of urinary tract infections in children. *Acta Paediatrica Scandinavica*, **61**, 390.

Boehm, J. J. and Haynes, J. L. (1966). Bacteriology of "midstream catch" urines. Studies in newborn infants. *American Journal of Diseases of Children*, **111**, 366-369.

Kunin, C. M., Zacha, E. and Paquin, A. J. (1962). Urinary tract infections in schoolchildren. I. Prevalence of bacteriuria and associated urologic findings. *New England Journal of Medicine*, **266**, 1287-1296.

Lincoln, K. and Winberg, J. (1964). Studies of urinary tract infections in infancy and childhood. II. Quantitative estimation of bacteriuria in unselected neonates with special reference to the occurrence of asymptomatic infections. *Acta Paediatrica Scandinavica*, **53**, 307-316.

Littlewood, J. M. (1972). Suprapubic aspiration of the urinary bladder. A comparative bacteriologic study. *Acta Paediatrica Scandinavica*, **61**, 390-391.

Lykken, K. B. and Grögaard, J. (1972). Suprapubic aspiration of the urinary bladder. A comparative bacteriologic study. *Acta Paediatrica Scandinavica*, **61**, 390-391.

Newman, C. G. H., O'Neill, P. and Parker, A. (1967). Pyuria in infancy, and the role of suprapubic aspiration of urine in diagnosis of infection of urinary tract. *British Medical Journal*, **2**, 277-279.

NORDEN, C. W. and KASS, E. H. (1968). Bacteriuria of pregnancy—a critical appraisal. *Annual Review of Medicine*, **19**, 431-470.

PRYLES, C. V. (1965). Percutaneous bladder aspiration and other methods of urine collection for bacteriologic study. *Pediatrics*, **36**, 128-131.

PRYLES, C. V., ATKIN, M. D., MORSE, T. S. and WELCH, K. J. (1959). Comparative bacteriologic study of urine obtained from children by percutaneous suprapubic aspiration of the bladder and by catheter. *Pediatrics*, **24**, 983-991.

ROBERTS, A. P., ROBINSON, R. E. and BEARD, R. W. (1967). Some factors affecting bacterial colony counts in urinary infection. *British Medical Journal*. **1**, 400-403.

SACCHAROW, L. and PRYLES, C. V. (1969). Further experience with the use of percutaneous suprapubic aspiration of the urinary bladder. Bacteriologic studies in 654 infants and children. *Pediatrics*, **43**, 1018-1024.

SMELLIE, J. M., HODSON, C. J., EDWARDS, D. and NORMAND, I. C. S, (1964). Clinical and radiological features of urinary infection in childhood. *British Medical Journal*, **2**, 1222-1226.

SMELLIE, J. M. and NORMAND, I. C. S. (1975). Bacteriuria, reflux, and renal scarring. *Archives of Disease in Childhood*, **50**, 581-585.

The Authors

J. D. Hardy, DObstRCOG, DCH, MRCP(UK), Senior Paediatric Registrar.

P. M. Furnell, MB, BS, Registrar in Medical Microbiology (now Assistant Microbiologist, Public Health Laboratory, Dulwich Hospital, London).

W. Brumfitt, MD, PhD, FRCP, FRCPath, Professor of Medical Microbiology.

Requests for reprints should be addressed to: Dr J. D. Hardy, 156 River Way, Loughton, Essex.

British Journal of Urology (1976), **48**, 284 ©

Short Case Report

A Knot in the Urethra

A 42-year-old unmarried man had made a habit for 2 years of masturbating by inserting a long plastic cord down his urethra into the bladder. Earlier he had used a straw but one day it escaped from his fingers and migrated to the bladder. A cystotomy was necessary to remove it. Since this accident he took a long cord which could not escape from his hands. One morning he entered the hospital because he could not extract the cord from his urethra. He had severe pain in the penis and presented with acute retention and serious urethral bleeding. A big haematoma had developed in the scrotum and penis. X-ray showed that the cord had knotted in the bladder and was pulled down into the penile urethra (Fig. 1). The knot was easily removed (Fig. 2) by a longitudinal, ventral incision in the penis but the urethra and corpus spongiosum were disrupted completely in their penile part, only the most distal end being intact. Bleeding was profuse. A perineal incision was necessary to repair the proximal part of the urethra which was traumatised but which could be conserved.

A new, scrotal hypospadiac meatus was made and the defect in the penile urethra was replaced by penile skin. A contraincision was performed on the dorsal side of the penis. An indwelling catheter was left in the bladder and a compressive bandage was applied around the penis. A reconstructive urethroplasty is planned.

Comment

Recently Irving Lissoos (1974) presented 3 cases of knots in the bladder. In 2 of them it resulted from catheterisation for acute retention, once with a filiform and once with a polythene tube. The complications were not as severe as in the present case. It is clearly demonstrated that a long flexible object, if passed too far in the bladder, can knot on itself. When extraction is tried serious complications may arise.

Wim Oosterlinck and Guy Renders
Department of Urology, University Hospital, De Pintelaan 135, B-9000 Ghent, Belgium

Reference

Lissoos, I. (1974). Knots in the bladder. *British Journal of Urology*, **46**, 346.

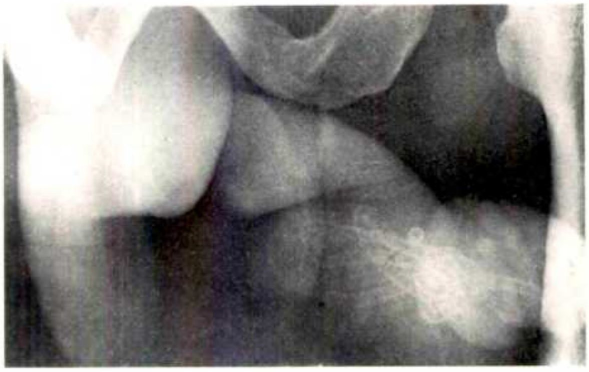


Fig. 1

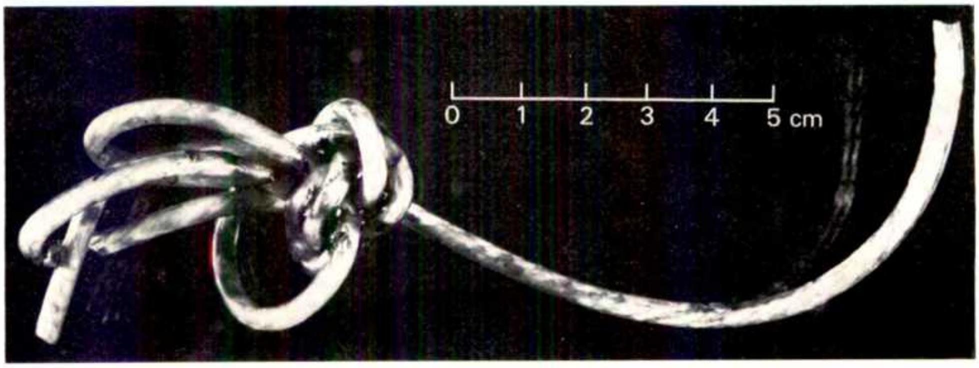


Fig. 2

British Journal of Urology (1976,) **48**, 285-291 ©

Comparison of Hydrophilic Polymer-coated Latex, Uncoated Latex and PVC Indwelling Balloon Catheters in the Prevention of Urinary Infection

M. J. TIDD, J. G. GOW, J. H. PENNINGTON, J. SHELTON and M. R. SCOTT

Division of Scientific Affairs, G. D. Searle and Co., High Wycombe and Sefton General Hospital, Liverpool

Indwelling urethral catheterisation is associated with risks of urinary infection and subsequent complications which increase with the duration of drainage (Miller *et al.*, 1960; Martin and Bookrajian, 1962; Kunin and McCormack, 1966). Bacteriuria has been substantially reduced by the adoption of closed aseptic drainage techniques but the reported incidence is still by no means negligible being 20% to 34% at 3 days (Brehmer and Madsen, 1972; Monson and Kunin, 1974) and up to 50% at 10 days (Kunin and McCormack, 1966). Attempts to obtain a further reduction of infection using antibiotic-impregnated catheters (Butler and Kunin, 1968) or intra-urethral lubrication with antibiotics (Kunin and Finkelberg, 1971) have also failed and since chemoprophylaxis is ineffective (Turck and Petersdorf, 1962; Gladstone and Robinson, 1968; Malek, Boyce and Wilkiemeyer, 1973) no substantial advance has been made since the original introduction of the closed aseptic drainage principle.

Although a report that the coating of indwelling urethral catheters with a hydrophilic polymer (Hydron) delayed the onset of significant bacteriuria (Lazarus *et al.*, 1971) was not confirmed in a subsequent investigation (Monson and Kunin, 1974), it seemed to us unwise to reject what might otherwise be a major development on the basis of a single investigation and we set out to compare urinary infection statistics obtained from Hydron-coated latex balloon catheters with those from otherwise identical uncoated catheters in a randomised statistically balanced experiment.

Since we were unable to find a publication comparing the urinary infection rates associated with latex catheters with those from catheters manufactured from the newer synthetic materials such as polyvinylchloride (PVC), silicone rubber, silicone-impregnated latex and polytetrafluoroethylene (PTFE) it seemed possible that any advantage to be gained from Hydron-coated latex over plain latex might still not represent an improvement over other materials. We therefore compared plain latex with a representative of the synthetics (PVC) as well as with Hydron-coated latex.

Objective

The objective was to investigate whether statistically significant differences in the incidence of infection could be demonstrated in urine sampled aseptically from male patients on closed aseptic catheter drainage with plain latex, Hydron-coated latex or PVC balloon indwelling urethral catheters.

Materials and Methods

(i) Subjects and Criteria for Admission to Study

The criteria for admission were deliberately kept to a minimum in order to obtain as large a number as possible of patients representative of the urological practice in which the study was performed. Male subjects only were selected. The other criteria were (*a*) the subjects were expected

Table I

Age of patients (years)	Type of catheter: Hydron-coated latex	Plain latex	PVC
20-29	1	0	0
30-39	0	0	0
40-49	0	1	2
50-59	3	1	3
60-69	8	7	5
70-79	4	7	6
80-89	1	0	1
Total number of patients	17	16	17
Mean (years)	64·0	66·8	65·0
Standard deviation (years)	13·5	8·5	10·3
Range	22-87	47-79	44-84

Mean ages not significantly different ($P > 0{\cdot}1$).

Table II

Diagnostic category	Type of catheter: Hydron-coated latex	Plain latex	PVC
Obstructive prostatic disease	14	11	13
Other	3	5	4
Total number of patients	17	16	17

The Chi-squared value did not achieve statistical significance ($P > 0{\cdot}1$).

to require an indwelling catheter connected to an aseptic closed drainage system for at least 72 hours, (*b*) the subjects were to be free of urinary infection at the time of admission and (*c*) no anti-microbial therapy had been administered within the 5 days prior to admission. Failure to insert the catheter without significant trauma or the subsequent discovery of significant infection in a catheter specimen of urine taken at the time of catheterisation disqualified the subject.

(ii) Catheters, Drainage System and General Procedure

All catheters were 18 French gauge with 20 ml balloon.

The PVC catheters were provided by J. G. Franklin and Sons. The latex catheters were produced by Warne's Surgical Products Ltd., and were specially coated with Hydron on the outside only. The catheters were connected to closed plastic drainage bags (Bardic No. 01612) by means of sterile pre-packed connector/samplers specially

Table III

		Type of catheter					
		Hydron-coated latex		Plain latex		PVC	
Specimen collection period	Definition of infection	Cumulative number infected	Cumulative % infection free	Cumulative number infected	Cumulative % infection free	Cumulative number infected	Cumulative % infection free
< 1 day	(1)	3	82	2	88	2	88
(specimen 2)	(2)	3	82	2	88	2	88
	(3)	3	82	2	88	4	76
1-2 days	(1)	7	59	7	56	9	47
(specimen 3)	(2)	8	53	7	56	9	47
	(3)	9	47	8	50	11	35
2-3 days	(1)	10	41	8	50	11	35
(specimen 4)	(2)	9	47	8	50	11	35
	(3)	11	35	10	38	12	29
3-4 days	(1)	12	27	12	25	12	29
(specimen 5)	(2)	12	27	12	25	12	29
	(3)	12	28	13	19	13	24
4-5 days	(1)	13	21	13	19	12	29
(specimen 6)	(2)	13	20	13	19	12	29
	(3)	13	21	13	19	15	12

manufactured for the study. Each connector contained a special latex rubber segment capable of withstanding many punctures by a fine gauge hypodermic needle passed obliquely through its wall. By clamping the drainage circuit below the sampler a urine specimen could be obtained aseptically immediately after it left the bladder without disconnecting the circuit. A urine specimen was obtained immediately following catheterisation. Subjects in whom this specimen was subsequently found to be infected were excluded from the study. The second and subsequent samples were obtained at approximately the same time of day, daily until the 5th day or until the catheter was removed, whichever was the sooner.

The Hydron coating required hydration before use to ensure flexibility. For this purpose 20 ml of sterile catheter lubricant (propylene glycol containing 1 : 2,000 chlorhexidine gluconate) was injected aseptically into the interior of the rigid plastic catheter pack a minute or so prior to use. The same procedure and lubricant was used with all types of catheter.

(iii) Laboratory Procedures

Urine samples were sent to the laboratory immediately and stored there at 4°C until cultured. Colony counts were made by serial dilutions being incorporated in pour plates of nutrient agar, and the characterisation of the growth by surface inoculation on 5% horse blood agar and cysteine, lactose electrolyte deficient (C.L.E.D.) agar. No attempt was made to identify species of coliform bacilli which fermented lactose, or coagulase-negative staphylococci and micrococci.

(iv) Statistical Design

Differences in catheter appearance made an open evaluation inevitable. A balanced design was used. The catheters were randomly allocated in subgroups of 3. Sealed envelopes were provided—each envelope indicating the order in which it should be opened. Following a decision to admit a subject the appropriate envelope was opened to determine the catheter to be used. In the event of a subsequent need to withdraw a subject because of urinary infection on admission, the next suitable subject was allocated to the same catheter type to maintain the balance of the experiment.

Results

(i) Comparability of Treatment Groups

Of the 54 patients who were admitted to the study, 4 (1 in each of the Hydron-coated and PVC groups, and 2 in the latex group) who were found subsequently to have had infected urine on admission were inadvertently not

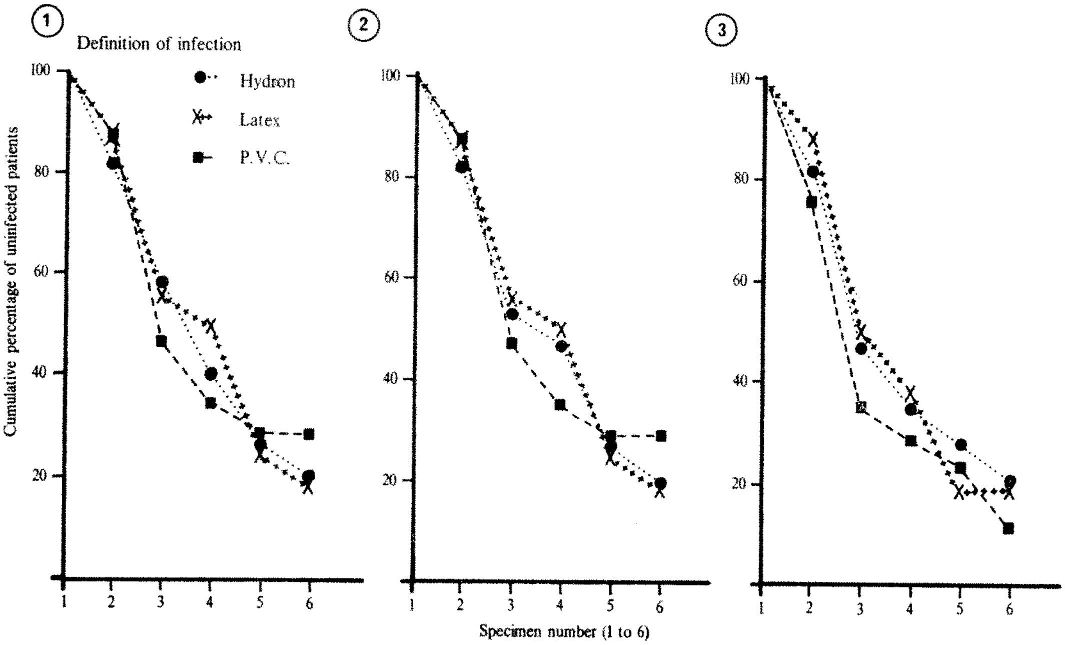


Fig. Cumulative percentage of patients remaining uninfected for 3 catheter types on 3 definitions of infection (see text).

replaced according to the protocol. The results presented relate to the remaining 50 patients. In 1 of these the balloon of a Hydron-coated catheter burst, necessitating its premature removal after the 4th specimen, which was uninfected, had been obtained. There is no reason to believe that the results have been appreciably biased as a result of these events. The distribution of the subjects between the various age and diagnostic categories within the 3 catheter groups is presented in Tables I and II. Testing by analysis of variance and Chi-squared procedures demonstrated that the 3 catheter groups were comparable in these respects.

(ii) Bacteriological Results

The interpretation of the bacteriological results is clearly influenced by the definition of 1st day of significant bacteriuria adopted. The data were examined using 3 different, though related, definitions of infection.

The first was identical with that used in an earlier investigation (Monson and Kunin, 1974), *i.e.* the day of first appearance of 10,000 organisms or more per ml of urine. The second defined the 1st day of infection as the day of first isolation of an organism which subsequently reached a concentration of 10,000/ml or more. The third was the 1st day of appearance of any organism isolated in any concentration. The cumulative numbers of infected patients and the cumulative percentage of infection-free patients in each treatment group are presented in Table III according to these 3 definitions. The data are plotted in actuarial life table form in the Figure.

It is apparent from the Figure that the proportion of patients remaining uninfected at any sample was similar for all the 3 catheter groups within each definition of infection. The infection rates for latex with and without Hydron coating were remarkably close together. The impression that the performance of the PVC catheters might have been appreciably inferior to that of the others was not confirmed. Formal statistical testing of the difference between the 3 curves in each set by the Chi-squared approximation to the logrank test (Peto and Pike, 1973) yielded non-significant values of Chi-squared demonstrating that their respective overall infection rates were statistically indistinguishable on all 3 definitions of infection employed. Although the most stringent definition of infection resulted predictably in the fewest patients remaining infection free, the differences produced in the results by the different definitions of infection were surprisingly small.

The overall results obtained confirm the earlier findings (Monson and Kunin, 1974) that Hydron-coating fails to confer any benefit in respect of the reduction of the probability of the

Table IV

	Type of catheter								
	Hydron coated latex			Latex			PVC		
Definition of infection:	1	2	3	1	2	3	1	2	3
Infecting organism									
None	4[a]	4[a]	4[a]	3	3	3	5	5	2
Coliform bacilli particularly									
Escherichia coli	5	5	4	2[b]	2[b]	3[b]	5	5	6
Proteus species	0	0	0	5[b]	5[b]	4[b]	0	0	0
Pseudomonas species	1	1	1	0	0	0	0	0	0
Alcaligenes faecalis	2	2	2	1	1	1	1	1	1
Staphylococcus aureus	0	0	0	2	2	1	1	1	1
Coagulase negative staphylococci and micrococci	3	3	4	1	1	2	2	1	5
Faecal streptococci	2	2	2	2	2	2	3	4	2
Yeasts	0	0	0	1	1	1	0	0	0
Total number of patients		17			16			17	

[a] Includes 1 patient, infection free at specimen 4, lost to follow-up (Balloon failed).

[b] 1 patient became infected for the first time in specimen 3 with *E. coli* and *Proteus*.

development of an infection. The results also showed that PVC catheters, whatever other benefits they may have, confer no advantage over latex in respect of propensity to infection during their use.

The results were examined for the possibility that although overall infection rates were similar there might be differences between catheter types in the frequencies of the various organisms grown, 1 catheter type perhaps favouring or inhibiting the growth of particular organisms.

The results, presented in detail in Table IV, demonstrate that regardless of the definitions of infection used there were no important differences between the catheter types in this respect either, with the possible exception of an excess of *Proteus* infections in the plain latex group. However, the small numbers involved prevented formal statistical testing of this point.

Finally, there being no demonstrable difference between the catheter groups, the results were pooled and examined for differences in the probability of infection being detected between different sampling times after the first 24 hours following catheterisation. The results were entirely consistent with a fixed probability of infection developing in a previously uninfected patient in the 24-hour period between the collection of 1 sample and the next, there being no statistically significant difference in frequency of infection in urine samples 3, 4, 5 and 6. Allowing for the effects of sampling variations this would give the approximately exponential decline in the number of infection-free patients with time which was observed.

Discussion and Conclusions

Although our results support the conclusions reached by Monson and Kunin (1974) the probability of an organism not being isolated in any urine sample following catheterisation was considerably higher in their study (about 92% overall) in contrast to about 74% in the study reported here although the same definition of infection was applied in each. On the assumption, consistent with our results, that after the second urine sample had been obtained there was a fixed probability (independent of catheter type) of infection developing in a previously uninfected urine in any 24-hour period between the collection of one sample and the next, the percentage (y) of uninfected patients remaining is given by $y = 100\,(1-p)^n$ where p is the fixed probability of an infection developing in any 24-hour period and n is the number of such periods elapsed. It can be seen that taken over a period of a few days the effects of small differences in p can become substantial. For example in this study nearly 80% of patients were infected after 5 days whereas Monson and Kunin (1974) experienced only a 35% infection rate after a similar period. It is difficult to avoid attributing this difference, at least in part, to the concomitant use of systemic antibiotics in nearly half of their patients. This may have reduced urinary tract infection or may have merely increased the difficulty of isolating organisms bacteriologically. None of our subjects received systemic antibiotics during the trial.

The failure of Hydron-coating to provide any useful effect is disappointing for it was expected that the excellent tissue compatibility and lubricating properties of the polymer, arising from its hydrophilic nature, would somehow affect the polymer/urethra interface in such a way as to reduce the likelihood of bacterial migration to the bladder from the exterior. This has proved to be unfounded.

Summary

Latex, hydrophilic polymer-coated latex and PVC balloon indwelling urethral catheters were compared in respect of the urinary tract infections arising in association with their use in male patients.

The polymer (Hydron) coating conferred no benefit over uncoated latex which in turn was indistinguishable from PVC.

No significant differences in the spectra of infecting organismns were observed between the 3 catheter types.

We wish to thank Mr D. E. Edwards for help with the design of this investigation and to record our appreciation of the technical assistance of Mr P. E. Cox and Miss Elizabeth Whitfield. We would also like to thank Smith and Nephew Research Ltd for applying the Hydron coating to the latex catheters.

References

BREHMER, B. and MADSEN, P. O. (1972). Route and prophylaxis of ascending bladder infection in male patients with indwelling catheters. *Journal of Urology*, **108**, 719-721.

BUTLER, H. K. and KUNIN, C. M. (1968). Evaluation of polymyxin catheter lubricant and impregnated catheters. *Journal of Urology*, **100**, 560-566.

GLADSTONE, J. L. and ROBINSON, C. G. (1968). Prevention of bacteriuria resulting from indwelling catheters. *Journal of Urology*, **99**, 458-461.

KUNIN, C. M. and FINKELBERG, Z. (1971). Evaluation of an intraurethral lubricating catheter in prevention of catheter-induced urinary tract infections. *Journal of Urology*, **106**, 928-930.

KUNIN, C. M. and MCCORMACK, R. C. (1966). Prevention of catheter-induced urinary-tract infections by sterile closed drainage. *New England Journal of Medicine*, **274**, 1155-1161.

LAZARUS, S. M., LA GUERRE, J. N., KAY, H., WEINBERG, S. and LEVOWITZ, B. S. (1971). A hydrophilic polymer-coated antimicrobial urethral catheter. *Journal of Biomedical Materials Research*, **5**, 129-138.

MALEK, R. S., BOYCE, W. H. and WILKIEMEYER, R. M. (1973). Urinary tract sterility and indwelling catheters. *Journal of Urology*, **109**, 84-85.

MARTIN, C. M. and BOOKRAJIAN, E. N. (1962). Bacteriuria prevention after indwelling urinary catheterisation. A controlled study. *Archives of Internal Medicine*, **110**, 703-711.

MILLER, A., LINTON, K. B., GILLESPIE, W. A., SLADE, N. and MITCHELL, J. P. (1960). Catheter drainage and infection in acute retention of urine. *Lancet*, **1**, 310-312.

MONSON, T. and KUNIN, C. M. (1974). Evaluation of a polymer-coated indwelling catheter in prevention of infection. *Journal of Urology*, **111**, 220-222.

PETO, R. and PIKE, M. C. (1973). Conservatism of the approximation $\Sigma(O-E)^2/E$ in the logrank test for survival data or tumor incidence data. *Biometrics*, **29**, 579-584.

TURCK, M. and PETERSDORF, R. G. (1962). Role of antibiotics in prevention of urinary tract infections. *Journal of Chronic Diseases*, **15**, 683-689.

The Authors

M. J. Tidd, MB., BSc, Director of Pharmacology, Division of Scientific Affairs G. D. Searle & Co. Ltd., High Wycombe (now Director of Clinical Research, Syntex Research Centre, Heriot-Watt University, Edinburgh).

J. G. Gow, MD., MCh, FRCS, Consultant Urologist, Liverpool Regional Urological Centre, Sefton General Hospital (now at Mossley Hill Hospital).

J. H. Pennington, MD, MRCPath, Consultant Bacteriologist, Sefton General Hospital.

J. Shelton, BSc, Senior Statistician, Division of Scientific Affairs, G. D. Searle and Co.

M. R. Scott, Research Associate, Division of Scientific Affairs, G. D. Searle and Co.

Correspondence and requests for reprints to: Dr M. J. Tidd, Syntex Research Centre, Heriot-Watt University, Riccarton, Edinburgh EH14 4AS.

British Journal of Urology (1976), **48**, 292 ©

Short Case Report

Ileal Replacement of Ureter of Solitary Kidney: 22-year follow-up

There are few reports of really late results of replacement of the ureter with a segment of ileum, particularly in a solitary kidney.

A 33-year-old woman was admitted because of bilateral lumbar pain for the previous 7 years. IVP showed bilateral strictures of the lower ureters. This was confirmed by bilateral retrograde uretero-pyelograms (Fig. 1). It was planned to replace both ureteric segments but at laparotomy the wall of the left ureter was found to be so thick that anastomosis with the ileal loop was considered inadvisable. A left cutaneous ureterostomy was performed. 2 months later the lower part of the right ureter was replaced with a segment of ileum, the ileo-ureteral anastomosis being side-to-side. During operation, retroperitoneal fibrosis was noted. Cystography after operation showed right ureteric reflux. A catheter in the left ureter is also seen. 5 years later the left kidney and ureter were removed.

In November 1975 the patient was re-admitted on account of cholelithiasis. She had worked hard ever since her previous operation. Urography (Fig. 2) and biochemical investigation showed satisfactory function of the solitary kidney. Multiple stones in the gall-bladder overlying the upper part of the kidney are shown. Cystoscopy showed a widely patent anastomosis between the bladder and the ileal segment.

Comment

Replacement of the ureter with a segment of ileum can manifestly be of long-term benefit; in the case described the patient has been very well and active for over 22 years.

STEFAN WESOLOWSKI
Department of Urology, Medical Academy Oczki, 6, Warsaw, Poland.

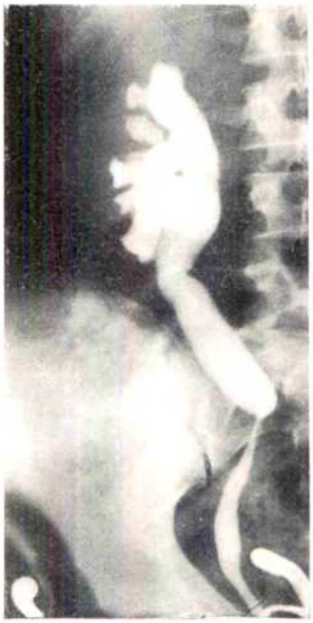


Fig. 1

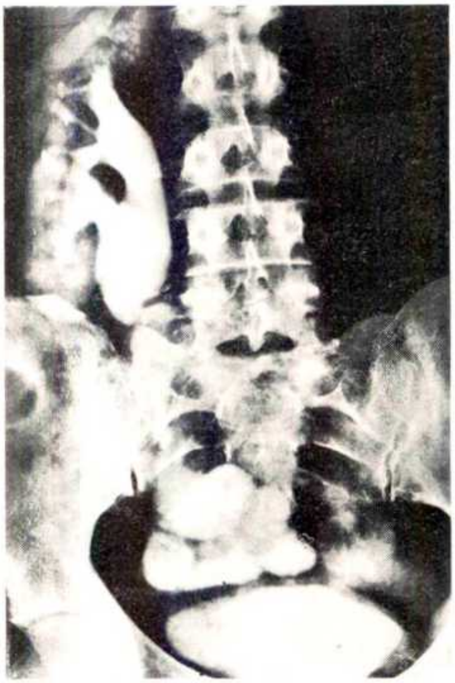


Fig. 2

British Journal of Urology (1976), **48**, 293 ©

Book Reviews

The Kidney—A clinico-pathological study. PRISCILLA KINCAID-SMITH. Pp. 454. Oxford: Blackwell. £18·50.

This is not a comprehensive textbook but a description of renal disease as seen by one individual in the forefront of clinical nephrology for the last 20 years. Half the 200-odd references are to the work of Dr Kincaid-Smith and her colleagues. None the less, it is a remarkable personal account. Dr Kincaid-Smith is one of the very few nephrologists who have remained their own histopathologist into the era of routine fluorescence and electron microscopy, and the very profuse, high-quality illustrations in this book show that she has mastered the new techniques as well as she explored the mysteries of light microscopy in the pioneer days of the 1950s. It is a fascinating account of nephrology written in the positive, stimulating style for which the author is well known and every nephrologist will want to own a copy or, at least, to recommend it to his local library. Urologists will not find so much of interest because the conditions which are not usually investigated by renal biopsy, such as obstruction and renal calculi, get short shrift; however, they will find the sections on end-stage renal failure and renal transplantation enlightening.

D. N. S. K.

Chemotherapy of Urogenital Tumours. Edited by GERALD P. MURPHY and ARNOLD MITTELMAN. Pp. 268+xiii, Tables 61, Figures 17. Springfield, Ill.: Thomas. 1975. $24·50.

Culling the world literature for the results of cancer chemotherapy is a thankless task. Reports concerning urogenital tumours are frequently to be found in obscure journals, mingled with large numbers of unrelated tumours and presented in such a way as to defy comparison with other data. The authors of this book have rendered a valuable service for they have succeeded in collating much of this important experience in a brief but comprehensive volume.

The specific cytotoxic and hormonal therapy of tumours of the kidney, urothelium, prostate, penis, testicle and adrenal are reviewed in turn, together with neuroblastoma, sarcomata and other rarities. There are a few surprising omissions, particularly from the British literature, but no review of this nature can be complete. The merits of single agents and multiple drug regimes are evaluated, and the advantages of combining drugs with radiotherapy and surgery discussed. The chapter on prostatic cancer illustrates the difficulties of establishing meaningful multicentre clinical trials and some of the attempts to overcome the problems. In general the presentation is of a high standard. Tables are useful but the text would benefit from the more generous use of sub-headings within chapters. The concluding chapter on animal models for chemotherapy evaluation is interesting, but fails to consider their relevance to the human clinical situation. Perhaps this very omission speaks for itself.

This book is recommended both as an aid for the urological oncologist and to deter the casual chemotherapist.

R. R. H.

Practical Cryosurgery. Edited by H. E. HOLDEN. 98 illustrations, 2 plates. Tunbridge Wells, Kent: Pitman. 1976. £5·00.

Mr Holden is to be congratulated on editing this small, well-illustrated book on cryosurgery together with eight other contributors with a known interest in this field of surgery. It should stimulate interest in those wishing to learn the technique and encourage others to seek guidance from those with expertise in cryosurgery.

It is practical in the sense that it reviews the scientific basis for the technique including the effect of "cold" on tissues and the engineering principles involved in the different types of apparatus. Good accounts are presented of the wide range of disorders in which cryosurgery has gained an accepted therapeutic place in the fields of ophthalmology, neurosurgery, gynaecology and general surgery. The editor correctly stresses in his preface that cases should not be treated indiscriminately, although the techniques are relatively simple.

The cryosurgical technique has not gained an accepted place in British urology and hence the use of a urological probe will be viewed with suspicion by many readers. No guidance is given on the duration of a prostatic freeze and the suggested combination of endoscopic resection a few days after cryosurgery may not commend the technique for its simplicity.

The account is, however, otherwise practical and concise, pointing to the possible future advances which may benefit the management of advanced cancer of the prostate and bladder.

N. A. G.

Announcements

PUIGVERT FOUNDATION, BARCELONA

The XL Annual International Urological Symposium will be held in Barcelona from 15 to 20 November 1976, and in Torremolinos, Spain, from 20 to 23 November 1976. Papers will be in English and Spanish. Simultaneous translation provided in Barcelona. Deadline for abstracts of free communications: 30 June 1976. Further details from Programme Secretary—N. Mallo, M.D., Fundacion Puigvert, Apartado 24005, Barcelona 13, Spain.

DIAGNOSTIC ULTRASOUND IN GASTROENTEROLOGY AND UROLOGY

The Department of Radiology, Gastroenterology and Urology of The Johns Hopkins Medical Institutions will present a Symposium on Diagnostic Ultrasound in Gastroenterology and Urology, 9 and 10 September 1976, at The Johns Hopkins Hospital. The programme is designed for the practising ultrasonographer, gastroenterologist and urologist. An in-depth coverage of the applications of diagnostic ultrasound to gastroenterology and urology will be provided. This course has been approved for 16 credit hours in Category I towards the Physician's Recognition Award of the AMA. The Faculty includes: D. Carpenter, B. Doust, T. Hendrix, F. Sample, R. Sanders, E. Smith, L. Von Micsky, P. Walsh and F. Winsberg. The fee is $150 (Resident and Technicians, $100). For registration forms and further details, write to Janet B. Hardy, M.D., Department of Continuing Education, The Johns Hopkins University School of Medicine, 720 Rutland Avenue, Room 17, Baltimore, Maryland 21205.

RECENT ADVANCES IN SURGICAL UROLOGY

Royal Postgraduate Medical School, Hammersmith Hospital, London, 25-29 October 1976

Topics include: The Prostate, Genital Infection, Urinary Diversion, Uropharmacology, Chemotherapy, Clinical Problems

Friday, 29 October, will be devoted to a special one-day course on Renal Transplantation. The Course is designed for Consultants, Senior Registrars and University Teaching and Research Staff.

Course Organisers: Mr G. D. Chisholm and Mr J. E. Castro.
Course Fee (for the entire week): £60 including lunch.
Course Fee (for Friday only): £14 including lunch.

These courses are approved for support under the Advanced Postgraduate Training Scheme.

Further details and application forms from:

The Deputy Secretary's Office
Royal Postgraduate Medical School, Hammersmith Hospital
Du Cane Road
London W12 0HS
Tel: 01-743 2030 Ext. 351

Conferences and Courses

UROLOGICAL SOCIETY OF AUSTRALASIA—PRELIMINARY COMMUNICATION

The Urological Society of Australasia will be holding its Annual Meeting in Perth, Western Australia, between 28th March and 1st April 1977.

INSTITUTE OF UROLOGY (UNIVERSITY OF LONDON)
in association with St Peter's Hospitals

Advance Notice of Meetings

Urology for the FRCS: 2-day course, 10th and 11th September 1976.
Postgraduate Nephrology: 2-day course, 9th and 10th November 1976.
The Management of Urinary Calculi: 1-day seminar, 13th November 1976.
Uro-Radiology Weekend: 2-day symposium, 10th and 11th December 1976.

For further details apply to the Secretary, Institute of Urology, 172 Shaftesbury Avenue, London, WC2H 8JE. Tel: 01 836 5361.

ABSTRACTS FROM CURRENT UROLOGICAL LITERATURE

Surgery Gynecology and Obstetrics

By Thomas Moore

"An Easy and Safe Technique for Nephrostomy." Chang-Ho Kim and Ole C. Fjeldborg. (1975, **141**, 95-96.)—The essence of the method of these Danish workers at the Transplantation Unit of Surgical Department T, University Hospital, Aarhus, is the use of a uterine sound passed through a small pyelotomy, a renal calyx and the cortex of the kidney. The nephrostomy tube is passed over the sound through the cortex into the pelvis to the correct site, the sound removed, the pyelotomy closed and the tubes fixed to the abdominal wall. When nephrostomy is necessary for rejection in a transplanted kidney, the sound can be passed from the pelvis with only a little lateral mobilisation of the kidney directly through a small wound in the abdominal wall and the tube threaded back along this into the pelvis. Before the nephrostomy tract has become fully epithelialised the tube can be changed by passing a ureteric catheter through it into the pelvis, removing the old tube and threading a new one into place over the catheter.

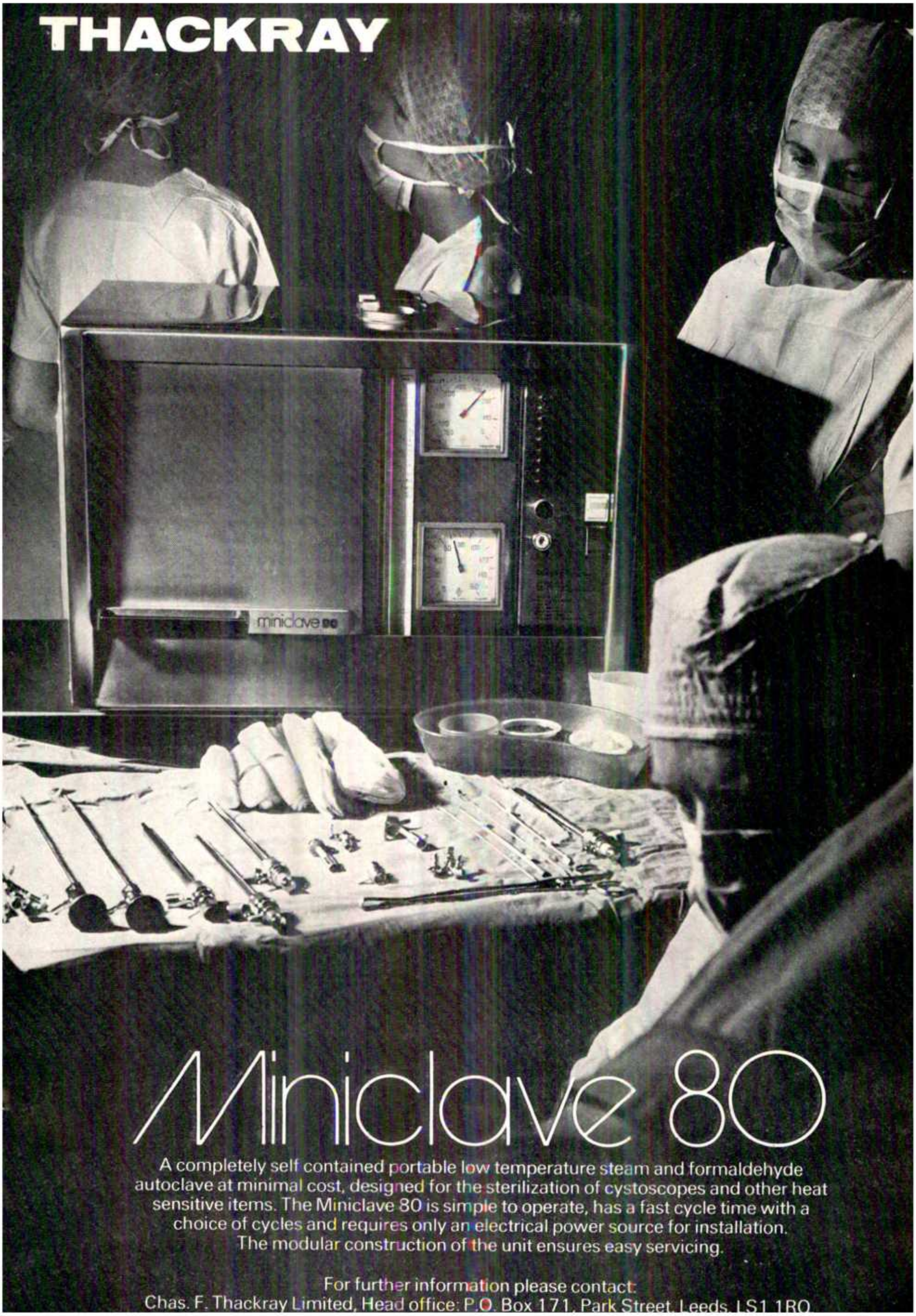
"Injuries of the Pelvic Ureter." Alan M. Smith. (1975, **140**, 761-764.)—From the New Cross Hospital, Wolverhampton, England, the author gives brief details of 6 cases of ureteric injury occurring out of a total of 5,500 abdominal gynecological operations. He stresses the value of preoperative urography to warn the surgeon of congenital and acquired anomalies of the ureter so that extra care is taken during operation. He also discusses the treatment the gynecologist should carry out in acute injuries found at operation and in later cases when no expert urological assistance is available.

"The effect of Suture Materials on Healing Wounds of the Bladder." J. Christopher Hastings, Walton Van Winkle, Ellen Barker, Dianne Hines and Waltraud Nichols. (1975, **140**, 933-937.)—From experiments carried out on dogs in the Department of Surgery of the University of Arizona Medical Centre, Tucson, the authors have shown bladder incisions gained 50% of tensile strength of normal in 21 days compared with stomach or colon wounds which gained no more than 70% in 120 days. Collagen synthesis was maximal in 5 days and returned to normal in 70 days, much quicker than similar wounds of stomach and colon where synthesis was still active even at 120 days. Silk and Mersilene sutures produced the greatest tissue reaction and, if exposed to the lumen of the bladder, stone formation occurred. This did not occur with monofilament polypropylene sutures. The tissue reaction was least with plain catgut but both it and the chromic variety were irregularly absorbed. Polyglactin-910 sutures were associated with tissue reaction of about the same degree as chromic catgut but were always absorbed between 28 and 70 days. They conclude, since the bladder is well healed by 21 days this is probably the ideal suture.

"Clinical Determinants of Survival from Postoperative Renal Failure." Se-Min Baek, Gilbert G. Makabali and William C. Shoemaker. (1975, **140**, 685-689.)—The authors report a prospective study of 114 consecutive cases of acute renal failure occurring in the intensive care unit of the Mount Sinai Hospital, New York. The overall mortality was 60% and 62% of all cases had a recorded episode of hypotension just before the failure developed. In 11 renal failure recurred following initial recovery. All of these patients died. The daily urinary output during the failure was inversely related to the mortality. The duration in this series was 11 to 12·4 days. In spite of the high mortality the authors regard acute renal failure, properly managed, as a benign, potentially reversible condition.

"Streptococcal Cellulitis of the Scrotum and Penis with Secondary Skin Gangrene." Beth Haury, George Rodeheaver, Thomas Stevenson, Carlos Bacchetta, Milton T. Edgerton and Richard F. Edlich. (1975, **141**, 35-39.)—The authors working in the Department of Plastic Surgery at the University of Virginia Medical Centre, Charlottesville record a case in a 63-year-old male. They quote and discuss in detail the relevant literature. The commonest organism is the beta-haemolytic streptococcus which causes oedematous swelling between Colles and Bucks fasciae with devacularisation of the overlying skin. Treatment consists of the necessary antibiotic therapy and relief of tension by relieving incisions. When gangrene occurs wide debridement followed by skin grafting is required.

Printed in Great Britain by T. & A. Constable Ltd, *Hopetoun Street, Edinburgh*



THACKRAY

Miniclave 80

A completely self contained portable low temperature steam and formaldehyde autoclave at minimal cost, designed for the sterilization of cystoscopes and other heat sensitive items. The Miniclave 80 is simple to operate, has a fast cycle time with a choice of cycles and requires only an electrical power source for installation. The modular construction of the unit ensures easy servicing.

For further information please contact:
Chas. F. Thackray Limited, Head office: P.O. Box 171, Park Street, Leeds, LS1 1RO

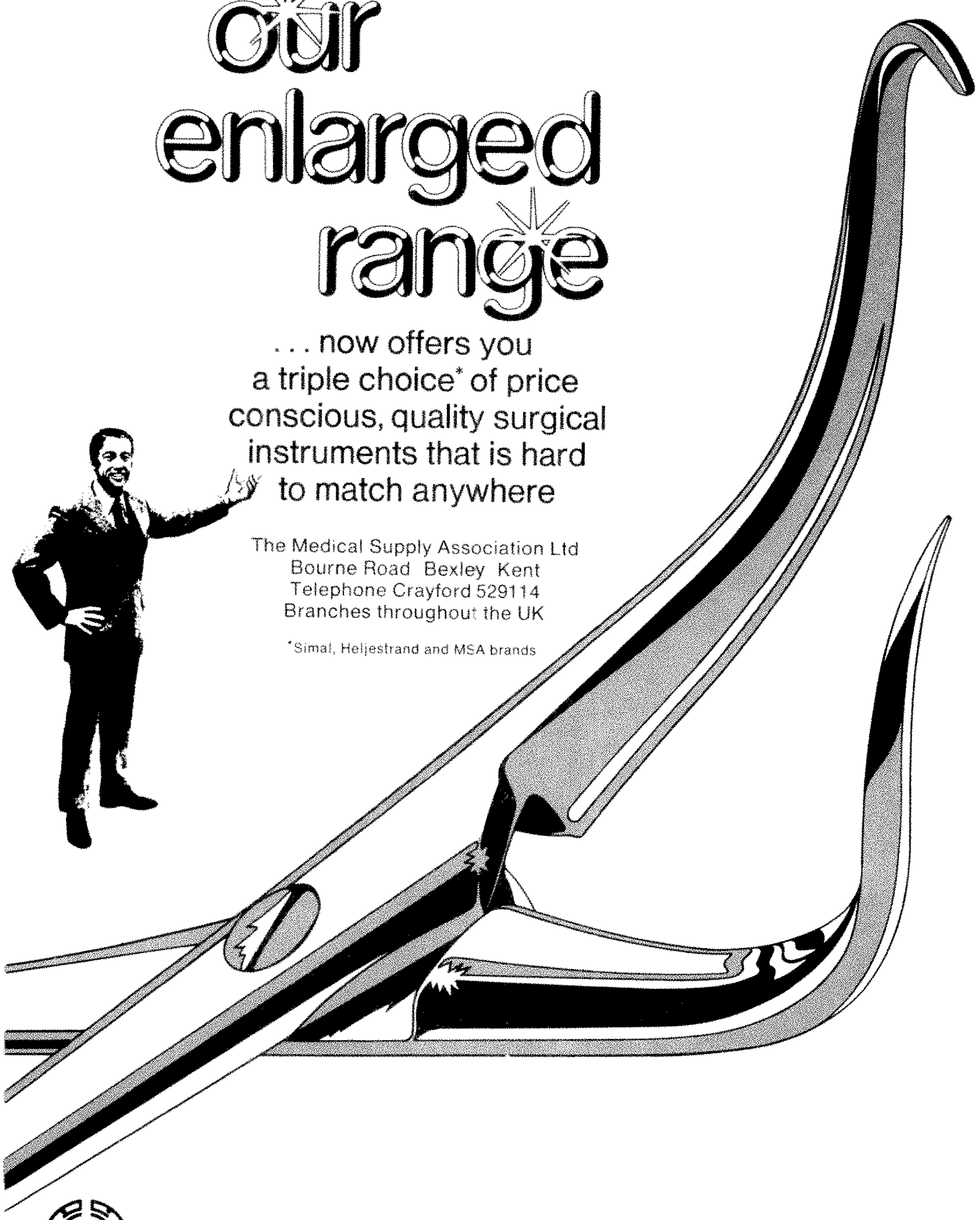
INS 2

our enlarged range

. . . now offers you a triple choice* of price conscious, quality surgical instruments that is hard to match anywhere

The Medical Supply Association Ltd
Bourne Road Bexley Kent
Telephone Crayford 529114
Branches throughout the UK

*Simal, Heljestrand and MSA brands



msa instruments in a big way

MANAGEMENT OF THE UROLOGICAL PATIENT

Robert Morpeth Jameson, K. Burrows and Beryl Large

1976 260 pages illustrated £4·75

This book explains the basic procedures encountered in the daily management of patients suffering from renal and genito-urinary disease. It is intended to supplement the standard text books as a manual of ready reference for use in the ward situation, and will be of value not only to those working on urological and renal units, but also to those being trained for such work.

For further details please contact:

Sales Promotion Department
Churchill Livingstone
23 Ravelston Terrace
Edinburgh EH4 3TL

If you would like to advertise in the British Journal of Urology please contact:

Sheila Devereux,
Advertisement Sales Executive,
Longman Group Ltd.,
Journals Division,
Longman House,
Burnt Mill,
Harlow,
Essex CM20 2JE

Telephone: Harlow 26721

Longman

BRITISH JOURNAL OF PLASTIC SURGERY

Official Journal of the British Association of Plastic Surgeons

Edited by T. Gibson

Since its inception in 1948 the Journal has maintained a consistently high standard and remains one of the leading international journals in its field. It circulates to over 80 countries and about two-thirds of its original articles are by overseas authors. Not only does it inform surgeons in other countries of the pioneer work done in Britain but it serves as an international forum for the exchange of new ideas from all over the world.

Published quarterly in January, April, July and October. Volume 29, 1976.

Annual subscription	£10·00	USA $27.00
Single numbers	£ 3·00	USA $ 9.00

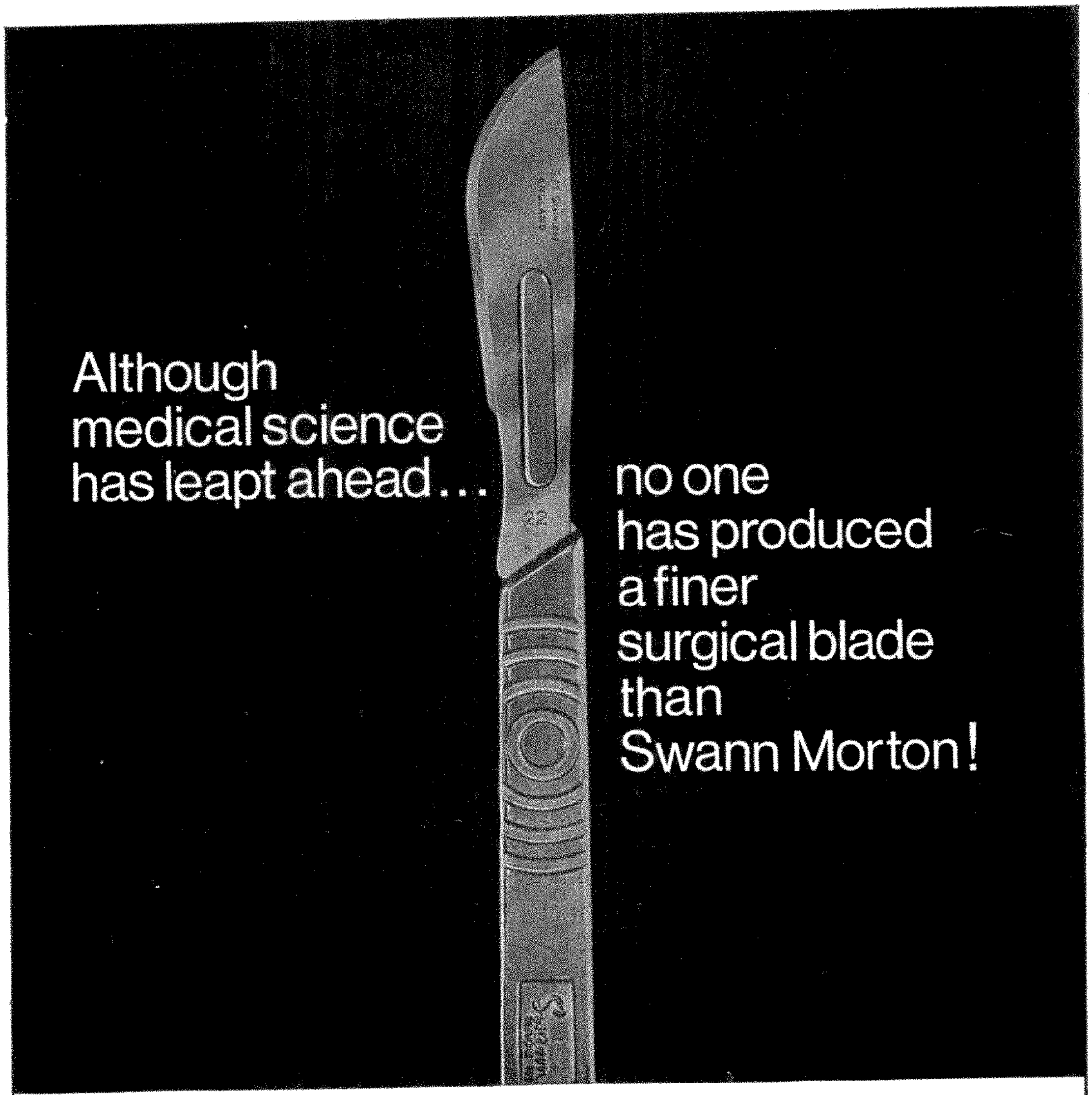
Subscriptions for USA should be sent to The Williams and Wilkins Company,
428 East Preston Street, Baltimore, Maryland, USA

Published under the E & S Livingstone imprint.

Subscription orders: Longman Group Ltd., Journals Division,
43/45 Annandale Street, Edinburgh EH7 4AT, Scotland.

All orders must be accompanied by the appropriate remittance.

Longman



Swann-Morton, the world's largest producers of surgical blades have kept abreast of the extremely high demands in surgical fields. Safe, stable and economical, their blades are sterilized by gamma radiation packed in quick peel foil envelopes and of a superb quality yet to be beaten.

STERILIZED
CARBON STEEL BLADES

STERILIZED
STAINLESS STEEL BLADES

STANDARD
CARBON STEEL BLADES

STERILE DISPOSABLE
STITCH CUTTERS

SURGICAL HANDLES

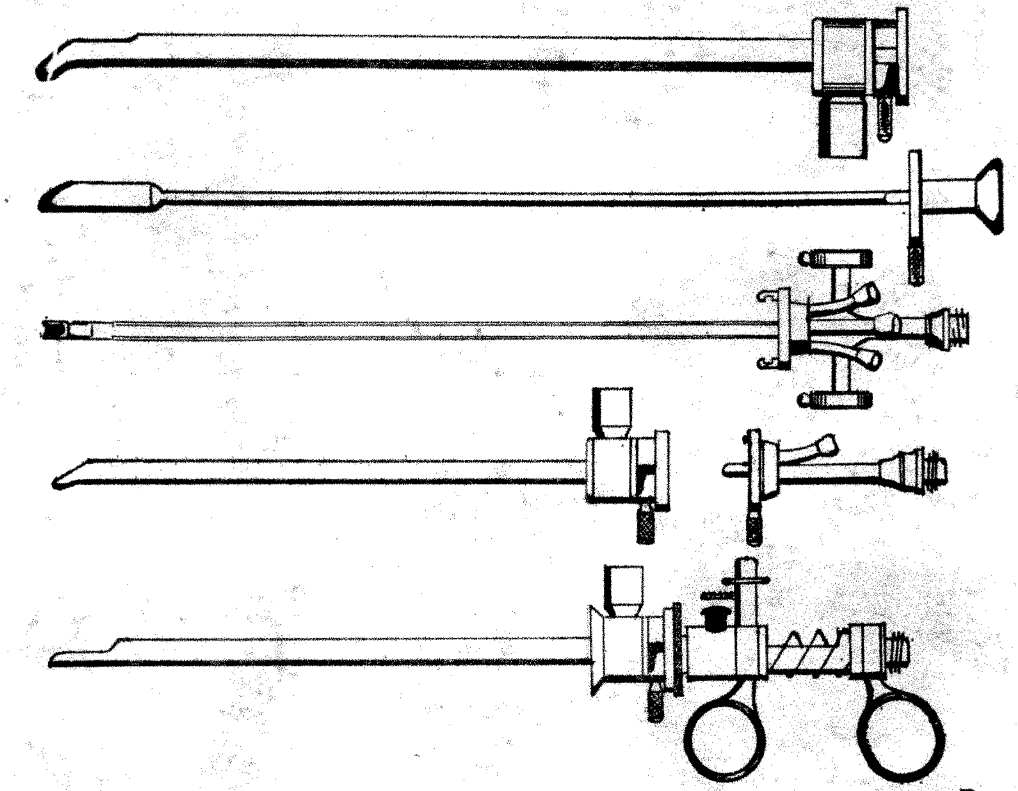
AUTOCLAVABLE PLASTIC
SURGICAL HANDLES

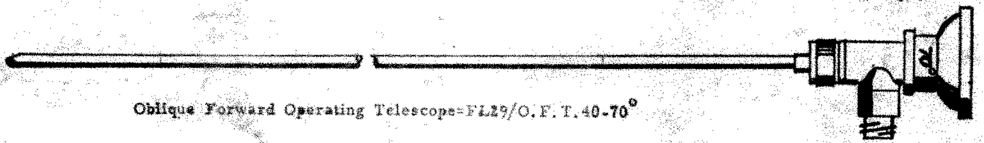
Swann-Morton

Surgical Blades

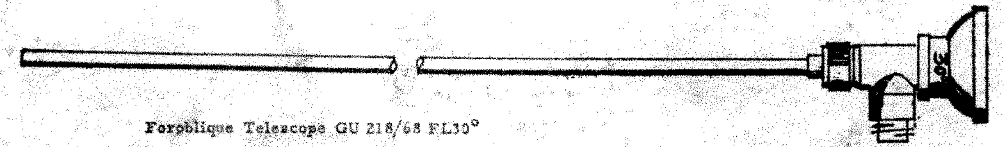
SWANN-MORTON LIMITED
PENN WORKS, OWLERTON GREEN,
SHEFFIELD S6 2BJ. ENGLAND

G.U. – BLANDY CYSTO-RESECTOSCOPE

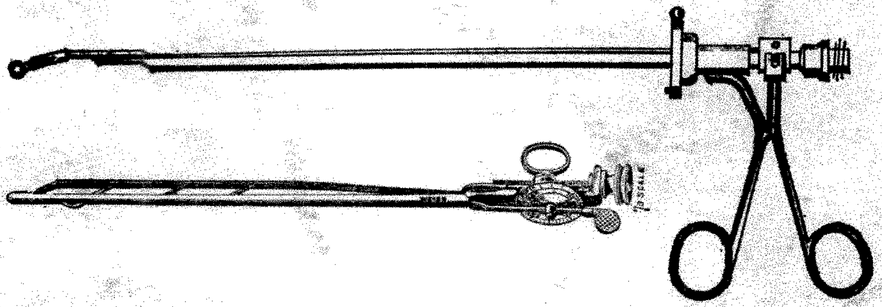




Oblique Forward Operating Telescope=FL29/O.F.T.40-70°



Forblique Telescope GU 218/68 FL30°



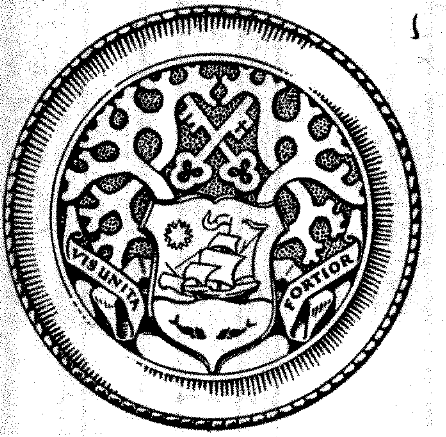
Made by
THE GENITO-URINARY MANUFACTURING CO. LTD.
28a 33–34 Devonshire Street London W1N 2AJ
Telephone:
01–935 2835/6/7
Telegrams:
Cystoscope London W1

ISSN 0007-133

15.11.77

BRITISH JOURNAL OF UROLOGY

Official Journal of the
British Association of Urological Surgeons



Volume 48 No 6

December 1976

E & S Livingstone

UNIVERSITY COLLEGE OF MEDICINE
LIBRARY

BRITISH JOURNAL OF UROLOGY

EDITOR
* W. KEITH YEATES

HON. TREASURER
* C. H. KINDER

ASSISTANT EDITORS
* G. D. CHISHOLM
* D. M. ESSENHIGH
* W. F. HENDRY
* W. SELBY TULLOCH

ASSISTANT EDITOR FOR AUSTRALASIA
G. F. MURNAGHAN

CONSULTING EDITORS
* DAVID BAND
* J. D. FERGUSSON

EDITORIAL COMMITTEE
Chairman D. INNES WILLIAMS*

M. HANDLEY ASHKEN, Norwich
G. H. BAINES, Birmingham
JOHN BALFOUR, Vancouver
D. R. BARNES, Cape Town
*J. P. BLANDY, London
JEAN CHARBONNEAU, Montreal
C. A. C. CHARLTON, Bath
PHILIP CLARK, Leeds
B. N. COLABAWALLA, Bombay
M. H. DEVEREUX, Loughton, Essex
J. N. de KLERK, Cape Town
E. CHARLTON EDWARDS, Manchester
E. J. ENGLAND, Perth, W. Australia
H. FINE, Durban
ALBAN H. GEE, Sydney
N. O. K. GIBBON, Liverpool
JOHN GRIEVE, Dundee
A. R. HARRISON, London
D. K. KARANJAVALA, Bombay
J. A. KENNEDY, Belfast
W. K. KERR, Toronto
KENNETH J. MACKINNON, Montreal
J. W. F. MACKY, Auckland
JOHN P. MADDERN, Adelaide
*J. P. MITCHELL, Bristol
*RICHARD A. MOGG, Cardiff
J. DERMOT O'FLYNN, Dublin
H. H. PEARSON, M.B.E., Canberra
J. S. PETERS, Melbourne
R. C. B. PUGH, London
P. J. M. RETIEF, Cape Town
CHARLES J. ROBSON, Toronto
L. STUART SCOTT, Glasgow
K. E. D. SHUTTLEWORTH, London
SARINDER MAN SINGH, Delhi
J. C. SMITH, Oxford
J. J. STEVENSON, London
*J. H. STEYN, Aberdeen
W. BARR STIRLING, Glasgow
JOHN SWINNEY, M.C., Bunbury, W. Australia
G. C. TRESIDDER, London
P. J. P. VAN BLERK, Johannesburg
DAVID M. WALLACE, O.B.E., London
J. G. WATSON, Brisbane
R. H. WHITAKER, Cambridge
*J. L. WILLIAMS, Sheffield
J. F. R. WITHYCOMBE, Cambridge
P. H. L. WORTH, London

* Members of Executive Committee

ST PETER'S MEDAL AWARDED TO

J. B. MACALPINE, 1949
R. OGIER WARD, 1951
TERENCE J. MILLIN, 1951
A. CLIFFORD MORSON, 1954
LESLIE N. PYRAH, 1959
CUTHBERT E. DUKES, 1960
DAVID BAND, 1962
SIR ERIC RICHES, 1964

THE BRITISH ASSOCIATION OF UROLOGICAL SURGEONS

ARTHUR H. JACOBS, 1965
D. INNES WILLIAMS, 1967
H. HAMILTON STEWART, 1968
JOHN SWINNEY, 1969
SIR MICHAEL WOODRUFF, 1970
D. S. POOLE-WILSON, 1971
DAVID M. WALLACE, 1973
A. W. BADENOCH, 1974
HOWARD G. HANLEY, 1975

E. & S. Livingstone
Edinburgh and London
December 1976

Contents

ORIGINAL ARTICLES

393 **The Ask-Upmark Kidney: A Form of Ascending Pyelonephritis?**
J. H. Johnston and L. W. Mix

399 **The Surgical Significance of the Proteus Stone**
W. K. Moores

403 **The Thermogravimetric Analysis of Renal Stones (in clinical practice)**
G. Alan Rose and C. Woodfine

413 **Allograft Nephrectomy**
S. N. Sinha and J. E. Castro

419 **Embolism in a Single Functioning Kidney: Report of Two Cases**
C. Selli, D. Turini and G. Berni

427 **Upper Urinary Tract Obstruction: Pressure/Flow Studies in Children**
H. N. Whitfield, N. W. Harrison, T. Sherwood and D. Innes Williams

431 **Preliminary Communication: Diagnosis of Gross Vesico-ureteric Reflux using Ultrasonography**
R. N. Tremewan, R. R. Bailey, P. J. Little, T. M. J. Maling, T. M. Peters and J. J. Tait

437 **Urinary Symptoms and Total Hysterectomy**
Anne M. Jequier

443 **The Real Bladder Electromyogram**
M. D. Craggs and J. D. Stephenson

453 **Nephrogenic Adenoma: a form of Adenomatous Metaplasia of the Bladder. A Clinical and Electron Microscopical Study**
E. A. Molland, P. A. Trott, A. M. I. Paris and J. P. Blandy

463 **Further Studies on Effects of Irrigation Solutions on Rat Bladders**
W. E. S. Harper and L. R. Matz

469 **A Reappraisal of the Pfannenstiel Incision**
David A. Griffiths

475 **Live Television Transmission of Transurethral and Open Pelvic Surgery with Reproduction on a Big Screen**
E. Zingg, R. Tscholl and K. Stief

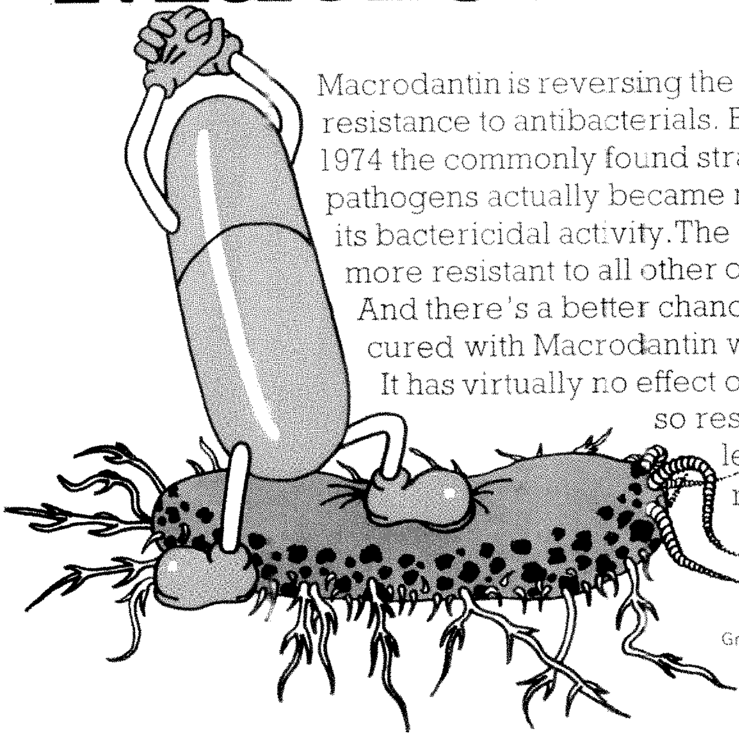
479 **The Value of Prophylactic Antibiotics in Transurethral Prostatic Resection: a Controlled Trial, with Observations on the Origin of Postoperative Infection**
Michael J. Morris, David Golovsky, Michael D. G. Guinness and P. O. Maher

485 **Testosterone Metabolism in Benign Prostatic Hypertrophy: *in vivo* Studies of Gestonorone Caproate and Cyproterone Acetate**
F. Orestano and J. E. Altwein

493 **Detrusor and Urethral Dysfunction in Prostatic Hypertrophy**
Jens T. Andersen and William E. Bradley

ISSN 0007-1331

more and more bacteria find they can't resist **Macrodantin**



Macrodantin is reversing the trend of increasing resistance to antibacterials. Between 1971 and 1974 the commonly found strains of urinary pathogens actually became more susceptible to its bactericidal activity. The organisms became more resistant to all other oral preparations.* And there's a better chance that the patient cured with Macrodantin will stay that way. It has virtually no effect on the bowel flora so resistant strains are less likely to develop re-infection and recurrence occur infrequently, if at all.

Grüneberg, R.N. (1976) *J clin. path.*, **29**, 292

An irresistible choice for treating U.T.I.

'Macrodantin' (nitrofurantoin macrocrystals)
is a registered trade mark.
Full information is available on request.
Eaton Laboratories, Regent House,
The Broadway, Woking, Surrey GU21 5AP

Macrodantin

MAja 1/10/6

499 **Artificial Insemination (A.I.H.) for Sperm Antibodies and Oligozoospermia**
M. McD. Usherwood, A. Halim and P. R. Evans

SHORT CASE REPORTS

402 **Contralateral Ureteric Metastasis from Renal Carcinoma**
M. A. Hughes, D. G. Arkell, P. Dawson-Edwards and J. R. Geddes

418 **Appendiceal Granuloma causing Bilateral Hydronephrosis and Macroscopic Haematuria**
K. Shimada, T. Katsumi and H. Fujita

426 **Filariasis Penis**
Shyam Prasad

436 **Appendico-vesical Fistula due to an Appendix Abscess with associated Goblet Cell Carcinoid of the Appendix**
M. di Paola and W. S. Stockwell

442 **Familial Profile of Transitional Cell Carcinoma**
S. K. Sharma, B. C. Bapna and S. M. Singh

452 **Long Survival after Vaginal Sarcoma Botryoides**
A. E. Stuart and J. Magri

468 **A Gynaecological Presentation of Phaeochromocytoma of the Urinary Bladder**
A. S. Whyte and A. Dick

478 **Urinary Retention due to Congenital Posterior Urethral Polyp in a Boy**
A. Ipiéns Aznar and J. M. Martinez-Peñuela V

492 **Obstructing Prostatic Urethral Calculi**
R. K. Vinson and S. A. Koff

498 **Testicular Metastasis from Prostatic Carcinoma**
N. P. Silverton

504 BOOK REVIEWS

504 ANNOUNCEMENTS

505 ABSTRACTS FROM CURRENT UROLOGICAL LITERATURE

franklin Simplastic foley catheters

the specialist system for everyday use...

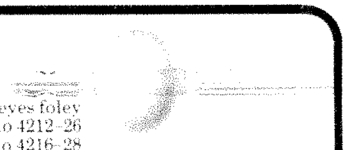
...the choice is yours

Specify Simplastic for all your needs. We supply a regular foley as well as coude tip/staggered eye, Tiemann tip, whistle tip, and continuous irrigation catheters, plus the special Gibbon designs.

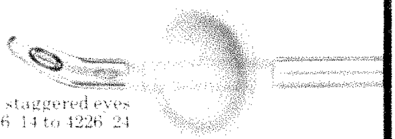
In the everyday situation when the catheterisation period is too short for silicone but too long for a latex catheter, Simplastic is the cost effective answer.

Simplastic resists encrustation, has excellent drainage powers and will stay in place longer without causing irritation to the mucosa.[1]

Simplastic means a dramatically reduced incidence of fluid absorption by the catheter.[2, 3]

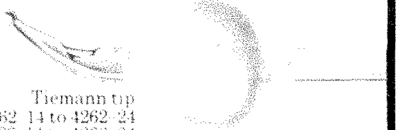


Two opposed-eyes foley
4212–12 to 4212–26
4216–14 to 4216–28

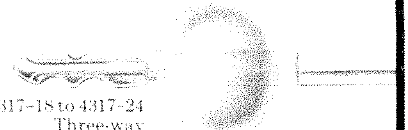


Coude tip staggered eyes
4226–14 to 4226–24

Whistle tip
4256–14 to 4256–28

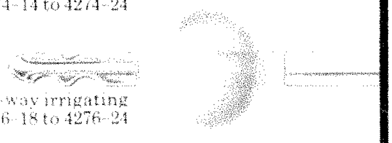


Tiemann tip
4262–14 to 4262–24
4266–14 to 4266–24



4317–18 to 4317–24
Three-way irrigating foley

Gibbon with two opposed eyes
4272–12 to 4272–24
4274–14 to 4274–24



Gibbon three-way irrigating
4276–18 to 4276–24

Simplastic Foley Catheters

1. Urology for Nurses, 1969, 234.
2. Lancet, Leading article, 1973, 1369.
3. PVC Technology, 1962, 126.

Simplastic is a Registered Trademark

J. G. Franklin & Sons,
P.O. Box 11 Coronation Road,
High Wycombe, Bucks. HP12 3TD.
A division of G. D. Searle & Co. Ltd.

Instructions to Authors

The *British Journal of Urology* welcomes original contributions on urological subjects from all parts of the world. The papers are accepted for consideration on the understanding that their contents have not been published in whole or in part elsewhere and that they are subject to editorial revision.

Any paper may be sent initially to a member of the Editorial Committee for comment and advice on its being suitable to be considered for publication.

A leaflet showing the criteria used in the assessment of papers submitted for consideration is available from the Editor on request.

Authors should supply their qualifications, main appointment, and the name and address of the hospital or the laboratory.

Please indicate name and address to which requests for offprints should be made.

Format and content of papers

The text of articles submitted for publication should be typewritten in double-spacing on paper sheet size 22 × 32 cm (A4). There should be a minimum margin of 3 cm all round. The pages should be numbered.

Reports on clinical or laboratory investigation should as far as possible be organised into the following main sections: (1) Introduction, (2) Objective(s), (3) Patients or Materials, (4) Procedures or Methods, (5) Findings or Results, (6) Discussion and (7) Conclusions with (8) a Summary at the end.

Nephrology. Papers on disorders of renal function of interest to the urological surgeon are welcome.

Ethics. When relevant, authors must include a statement on the ethical aspects of their research.

Reports of clinical cases should consist of the following sections: (1) Introduction, (2) Case Reports and (3) Comment with (4) a Summary at the end.

Reports on single cases. Papers reporting a single case are considered for publication as full papers only when the case has definite instructional value. The Introduction and Discussion should not be disproportionate to the case presentation. *An abbreviated version suitable for publication as a Short Case Report as an alternative must also be submitted.*

In all full papers the literature should be summarised as concisely as is consistent with establishing the necessary basis for new material. Discussion and Conclusions should be strictly limited to the results presented. Recapitulation from previous sections should be avoided whenever possible. Summaries should be composed of very brief statements about each of the main sections.

Headings. The relative importance of sub-headings should be clearly indicated.

Numbers. All numbers should be shown as figures rather than as words.

References. *The accuracy of references is the responsibility of the author.* Only papers closely related to the author's work should be referred to; exhaustive lists should be avoided. *References in the text* should be quoted by the author's name(s) and year of publication. Unless there are more than 3 authors, all the names should be stated at the first reference; if there are more than 3 authors only the first author plus *et al.* is used. In subsequent references to the same paper, *et al.* is used if there are more than 2 authors. *The list of references at the end of the paper* should be in alphabetical order. *References to Journals* should include the name(s) and initials of the author(s), year, title of paper, name of journal in full, volume number and the numbers of the first and last pages, *References to books* should include the name and initials of the author, year, title of book, number of edition, city of publication, name of publishing house, and page number(s).

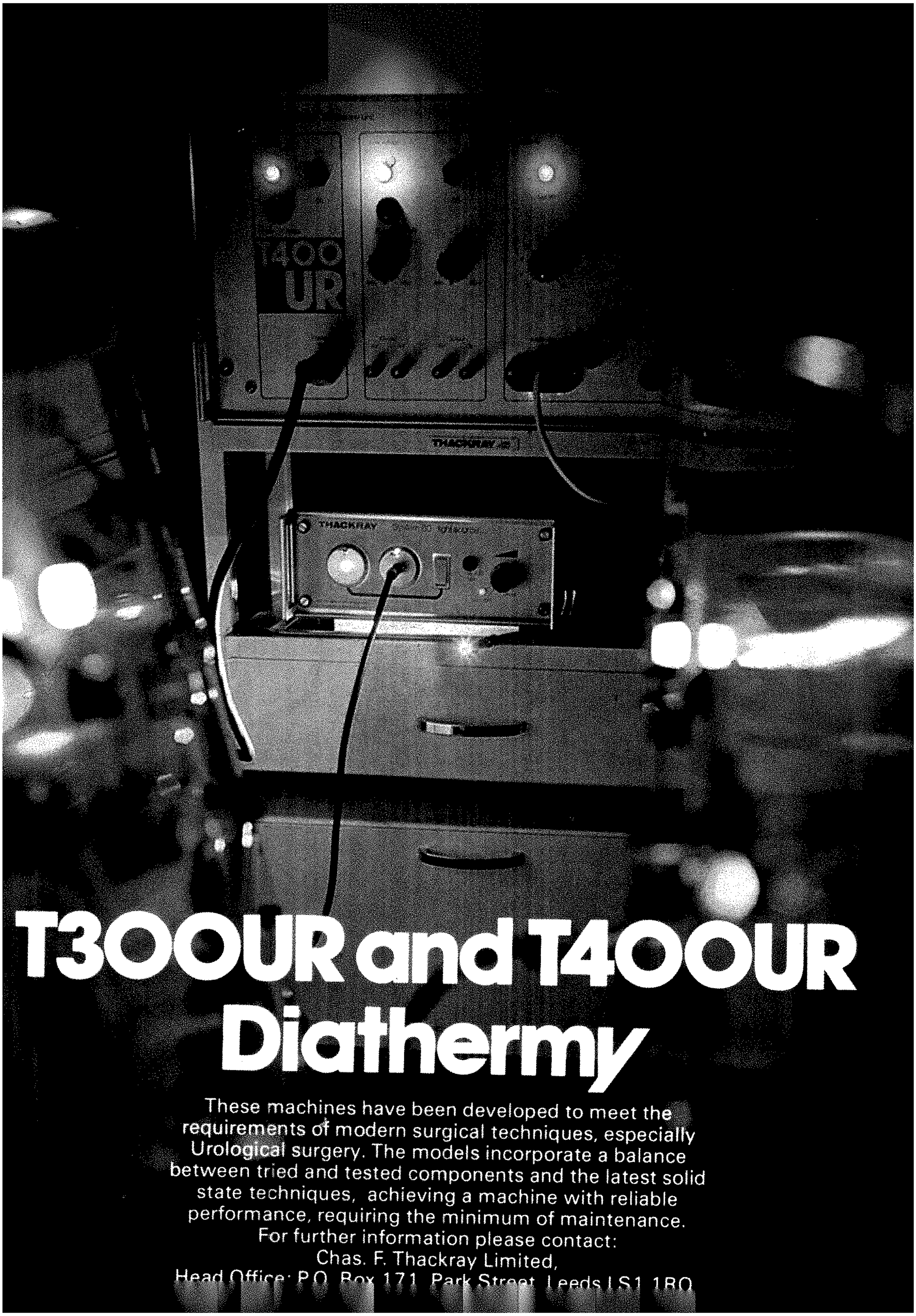
Illustrations. Photographs and radiographs should be submitted in the form of *matt* prints of a size no larger than 17·5 × 12·5 cm and no smaller than 9 × 6·5 cm. All figures should be sent unmounted. The number of the figure, the name of the author and the "top" of the illustration should be indicated lightly in pencil on the back. The magnification of micro-photographs should be stated. Graphs and diagrams should be drawn in Indian ink. *Lettering and figures must be indicated only on a transparent cover.* Legends to figures should be typewritten on a separate sheet of the manuscript. Tables, unless they are very small, should also be typewritten on separate sheets. The position of illustrations and tables should be indicated in the margin of the text.

There is no charge to contributors for the printing of black-and-white illustrations on papers accepted for publication. Illustrations in colour may be accepted at the discretion of the Editor provided he is of the opinion that these are necessary for the improvement of the article The author may be required to pay for the extra cost involved by the reproduction in colour.

Offprints

25 offprints are supplied to the first named author only, free. Forms for ordering offprints will be sent with the proofs for correction; the order form should be returned with the corrected proofs within 7 days.

Continued on page vii



T300UR and T400UR Diathermy

These machines have been developed to meet the requirements of modern surgical techniques, especially Urological surgery. The models incorporate a balance between tried and tested components and the latest solid state techniques, achieving a machine with reliable performance, requiring the minimum of maintenance.

For further information please contact:
Chas. F. Thackray Limited,
Head Office: P.O. Box 171, Park Street, Leeds LS1 1RQ

Travelling Fellowship

The British Association of Urological Surgeons offers a Travelling Fellowship of £250 based on the best paper published in the *British Journal of Urology* in the preceding year including those papers presented at the British Association of Urological Surgeons Annual Meeting.

Candidates for the prize must be Fellows of one of the Royal Colleges of Surgeons in the British Isles, Canada, Australasia or South Africa who are in the course of urological training or who have obtained consultant posts within 10 years of the date of submission of the paper.

Authors of papers with multiple authorship should indicate which one of their number should be awarded the Fellowship in the event of their contribution being selected.

Three assessors will be appointed by the Council to make recommendations on the award of the Fellowship. The Council reserves the right not to make an award in any one year.

The award will be announced at the June meeting of the Association.

Short Case Reports

Brief reports (preferably with 1 and not more than 2 illustrations) of unusual cases not published elsewhere may be submitted as summaries of not more than 200 words for consideration for publication as Short Case Reports. They should comprise (1) a Title, (2) Case description and (3) a brief Comment. The authors and references are each limited to 3. The titles of these reports will usually be recorded in Index Medicus and by MEDLARS.

Preliminary Communications

Preliminary communications of original work may be submitted as short papers. The communication should be divided into 4 sections: (1) Objectives, (2) Materials and Methods, (3) Preliminary results, (4) Interpretation or Significance of Results.

Discussion of Papers

Questions or criticisms concerning recently published papers' may be sent to the Editor, who will refer them to the authors. The readers' comments and authors replies may subsequently be published together.

There is no other correspondence section in the Journal.

Suggested Projects for Urological Research

Clinicians who have ideas for research projects, but have no opportunity for carrying them out, may submit them for publication in the above section. The communication should not be longer than 500 words. References will be limited to 6.

Abstracts from Current Urological Literature

Urologists who are willing to undertake abstracting of urological articles appearing in other journals should communicate with the Assistant Editor, Mr. W. Selby Tulloch, at the Department of Urology, Western General Hospital, Edinburgh, EH4 2XU.

Addresses

With the exceptions noted below, all editorial communications, including books for review, should be addressed to the Editor. Mr. W. Keith Yeates, at the Department of Urology, Newcastle General Hospital, Newcastle upon Tyne, NE4 6BE.

Preliminary Communications on Research Projects and *Suggested Projects for Urological Research* should be submitted to the Assistant Editor, Mr G. D. Chisholm, at the Urology Unit, Hammersmith Hospital, Royal Postgraduate Medical School, London, W12 0HS.

Short Case Reports (presented as described above) should be sent to the Assistant Editor, Mr W. F. Hendry, Institute of Urology, University of London, 172 Shaftesbury Avenue, London, WC2H 8JE.

Communications concerning the Abstract Section should be sent to the Assistant Editor, Mr W. Selby Tulloch, at the Department of Urology, Western General Hospital, Edinburgh, EH4 2XU.

Publishing, Advertisement and other enquiries: E. & S. Livingstone, Longman Group Ltd., Journals Division, Longman House, Burnt Mill, Harlow, Essex CM20 2JE.

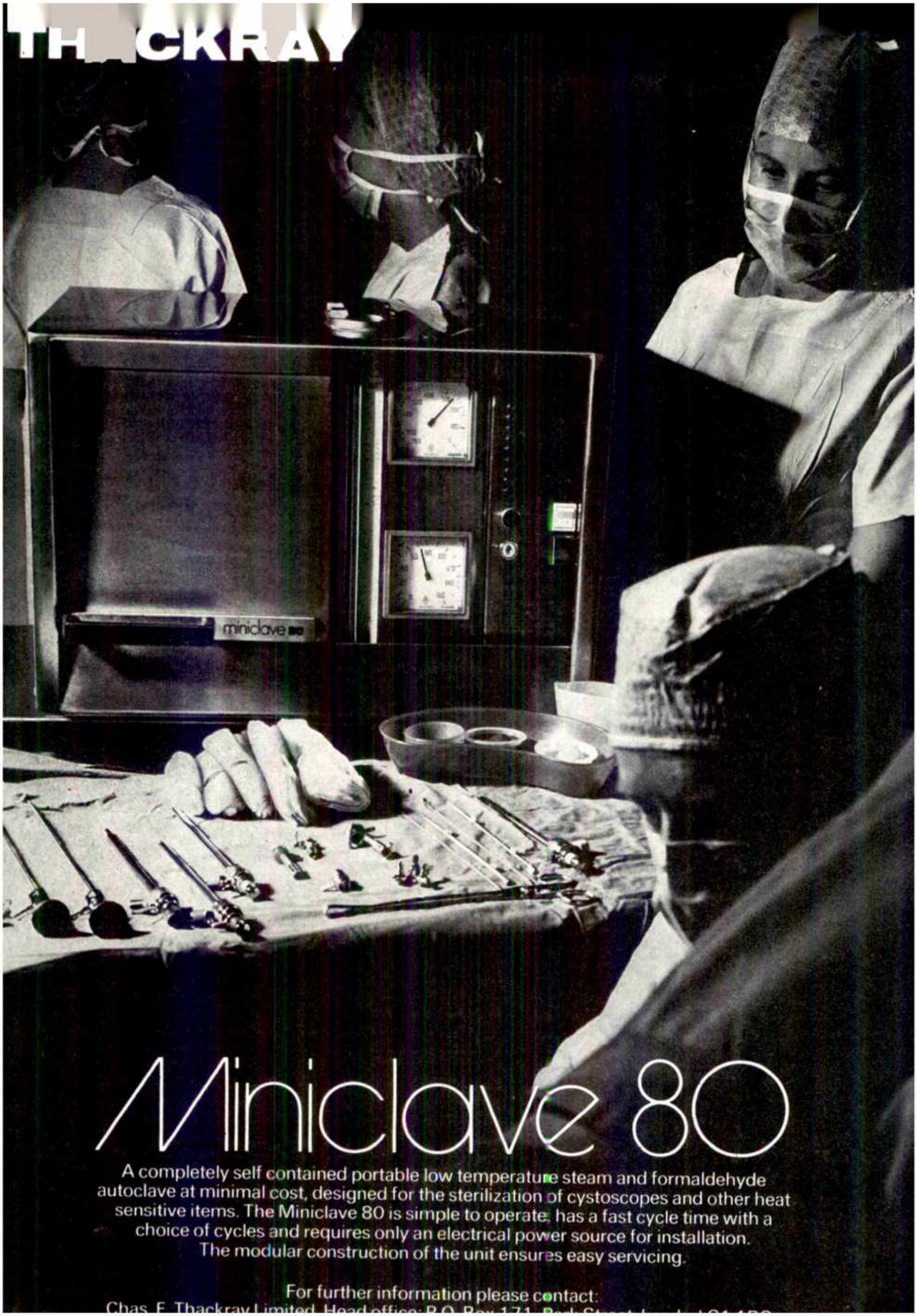
Subscriptions

The Journal is published in February, April, June, August, October and December. Volume 48, number 7, is included in the subscription price and publishes the papers presented at the 1976 B.A.U.S. Conference. Subscription £17·00 (U.S.A. $45.00) per annum, post free. Single copies £3·00 (U.S.A. $7.50) each. Previous volumes and parts of volumes (if available) may be obtained from the publishers, price £6.00 per volume or 75p for single parts.

Subscription enquiries: Messrs E. & S. Livingstone, Journals Division, 43/45 Annandale Street, Edinburgh, EH7 4AT.

Subscriptions for U.S.A. should be sent to The Williams and Wilkins Company, 428 East Preston Street, Baltimore, Maryland, U.S.A.

© 1976. All rights reserved. No part of this publication may be reproduced, stored in a retrieval system, or transmitted in any form or by any means, electronic, mechanical, photo-copying, recording or otherwise, without the prior permission of the copyright owner.



THACKRAY

Miniclave 80

A completely self contained portable low temperature steam and formaldehyde autoclave at minimal cost, designed for the sterilization of cystoscopes and other heat sensitive items. The Miniclave 80 is simple to operate, has a fast cycle time with a choice of cycles and requires only an electrical power source for installation. The modular construction of the unit ensures easy servicing.

For further information please contact:
Chas. F. Thackray Limited. Head office: P.O. Box 171, Park Street, Leeds LS1 1RQ

AN IMPORTANT ANNOUNCEMENT FROM MAY & BAKER:

A MAJOR, NEW INDICATION FOR 'FLAGYL'

the treatment and prevention of anaerobic infections

Modern methods reveal the size of the problem
Sophisticated laboratory techniques now show the true incidence of anaerobic infections. Increasingly, these organisms are isolated from clinical specimens,[1] and are implicated in a wide variety of infections.[1-3]

'FLAGYL' is the dependable answer
Free from the problems associated with other agents in this field (eg chloramphenicol) and, unlike penicillin, active against both sporing and non-sporing forms – 'Flagyl' is bactericidal to most of the clinically important, obligatory anaerobes.[1] 'Flagyl' has been used successfully in the following conditions: pelvic,[4] intra-abdominal[5] and post-operative[4] infections, brain abscess[6] septic thrombophlebitis[7] and necrotizing pneumonia.[8]

Positive benefits to the hospital unit
". . . it may be concluded that the prophylactic use of metronidazole ('Flagyl') in the test group resulted in a saving to the N.H.S. of almost £2,000 . . . prevention of anaerobic infection enabled the gynaecological ward to handle an additional 26 major surgical cases each year."[4]

Backed by an unrivalled reputation
'Flagyl' has an outstanding record of efficacy and safety in over 15 years of clinical experience. It is now firmly established in the treatment of urogenital trichomoniasis, amoebiasis, giardiasis and acute ulcerative gingivitis.

References
1. *Drug and Therapeutic Bulletin*, **14**, 25, 1976
2. Phillips, I. and Sussman, M. p.37 *Infections with Non-Sporing Anaerobes* Published Churchill
3. Study group, *Lancet*, **ii**, 1540, 1974
4. Study group, *J. Antimicrobial Chemotherapy*, **1**, 393–401, 1975
5. Willis, A.T., *et al.*, *Br.Med.J.*, February 7, **i**, 318–321, 1976
6. Ingham, H.R., *et al.*, *Br.Med.J.*, **iv**, 39, 1975
7. Mitre, R.J. & Rotheram, E.B., *J.Amer.Med.Assoc.*, **230**, 1168, 1974
8. Tally, F.P., *et al.*, *Antimicrobial Agents & Chemotherapy*, **7**, 672, 1975

'Flagyl'* is supplied as tablets of 200 mg and tablets of 400 mg. Full prescribing information on request
*trade mark of May & Baker Ltd Dagenham Essex RM10 7XS for its preparations of metronidazole.

M&B May&Baker

A member of the
Rhône-Poulenc Group of Companies

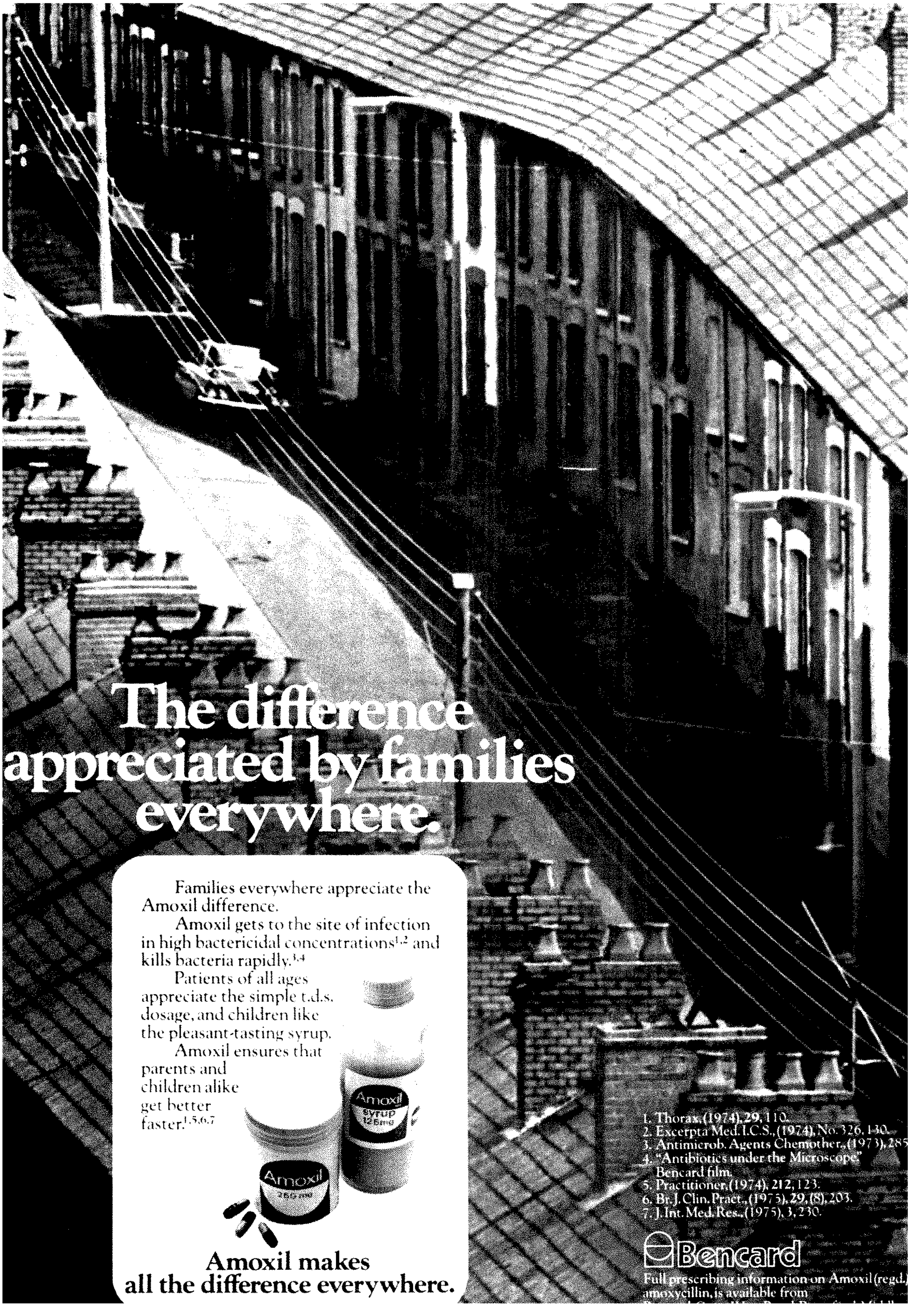
MA4576

System 80

A modular range for examination, catheterisation and resection. The system is built around the clarity of a rod lens telescope and manufactured to B.A.U.S. specification in accordance with patent number 954 629.

A well proven 24 hours telescope repair service is available in the U.K. when necessary.

For further information please contact: Chas. F. Thackray Limited.
Head Office: P.O. Box 171, Park Street, Leeds LS1 1RQ



Families everywhere appreciate the Amoxil difference.

Amoxil gets to the site of infection in high bactericidal concentrations[1,2] and kills bacteria rapidly.[3,4]

Patients of all ages appreciate the simple t.d.s. dosage, and children like the pleasant-tasting syrup.

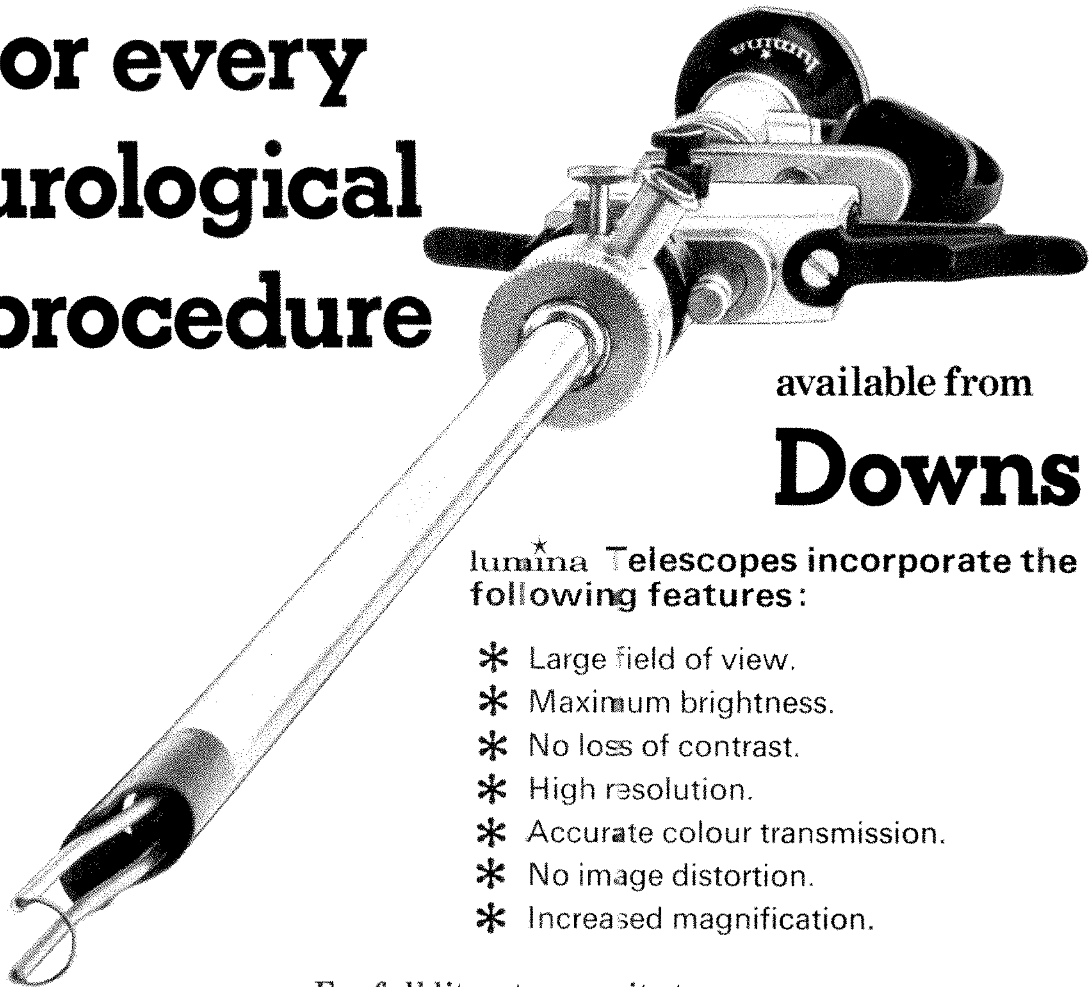
Amoxil ensures that parents and children alike get better faster.[1,5,6,7]

Amoxil makes all the difference everywhere.

1. Thorax,(1974),29,110.
2. Excerpta Med.I.C.S.,(1974),No.326,130.
3. Antimicrob.Agents Chemother.,(1973),285
4. "Antibiotics under the Microscope." Bencard film.
5. Practitioner,(1974),212,123.
6. Br.J.Clin.Pract.,(1975),29,(8),203.
7. J.Int.Med.Res.,(1975),3,230.

Bencard

Full prescribing information on Amoxil (regd.) amoxycillin, is available from



WOLF lumina®

Endoscopes for every urological procedure

available from

Downs

lumina Telescopes incorporate the following features:

- * Large field of view.
- * Maximum brightness.
- * No loss of contrast.
- * High resolution.
- * Accurate colour transmission.
- * No image distortion.
- * Increased magnification.

For full literature, write to:

Downs Surgical Ltd
CHURCH PATH, MITCHAM, SURREY
CR4 3UE Tel. 01-640 3422 & 01-648 6291

In Radiography

Conray Contrast Media

Products of distinction in their substance and shadow

'Conray' contrast media are formulations of either meglumine iothalamate, sodium iothalamate or combinations of the two. These high iodine/low viscosity preparations have an established record of excellence in providing wide margins of safety and tolerance for the patient together with optimum visualization in a comprehensive range of radiographic procedures.

Full information on 'Conray' 280, 'Conray' 325, 'Conray' 420, Cardio-'Conray', Retro-'Conray' and Gastro-'Conray' supplied on request to May & Baker Ltd Dagenham Essex RM10 7XS

*trade mark of Mallinckrodt Inc.

Conray*
Contrast Media–
A salt for all reasons
A view of all regions

M&B May & Baker

A member of the Rhône-Poulenc Group of Companies

MA 3132

CHARLES C THOMAS • PUBLISHER

CLINICAL ASPECTS OF UREMIA AND DIALYSIS *edited by* **Shaul G. Massry** *and* **Alvin L. Sellers**, *both of the Univ. of Southern California School of Medicine, Los Angeles. Foreword by* **George E. Schreiner.** *(40 Contributors)* A totally comprehensive and up-to-date description of the various aspects of the uremic syndrome and its effect on the different organs is presented in this book. Neurological, cardiovascular, hematopoietic, gastrointestinal and metabolic changes are emphasized and a thorough assessment of all the diverse techniques, forms and styles of dialysis as they are practiced today is included. *'76, 768 pp. (6 3/8 x 9 5/8), 264 il., 80 tables, $59.75*

RENAL CALCULI: A Guide to Management *edited by* **William C. Thomas, Jr.**, *Univ. of Florida, Gainesville. Foreword by* **John E. Howard.** *(3 Contributors)* Information in this book encompasses the management of most of the different types of kidney stones, concentrating on that which is of practical value in the control of calculi. Included is a discussion of clinical settings in which various tones are most likely to occur, the physical and radiographic appearance of the more common stones, determination of the type of stone being formed, and documentation of pertinent events in the medical history. *'76, 192 pp., 62 il., 11 tables, $15.50*

CHEMOTHERAPY OF UROGENITAL TUMORS *by* **Gerald P. Murphy** *and* **Arnold Mittelman**, *Roswell Park Memorial Institute, Buffalo, New York. Foreword by* **Willet F. Whitmore, Jr.** *(4 Contributors)* This book presents a comprehensive review of past achievements in chemotherapy, presents uses and results of this therapy, and areas for future advancement. Each chapter features a realistic and critical evaluation of the clinical usefulness of chemotherapy in all stages and types of urogenital cancer, outlining representative programs. Within each disease category, criteria for evaluation of the clinical benefit of chemotherapy are presented and analyzed. *'75, 288 pp., 15 il., 62 tables, $24.50*

UROLOGICAL RADIOLOGY OF THE ADULT MALE LOWER URINARY TRACT: Anatomy, Physiology, Pathology and Sequelae, Diagnosis and Management *by* **R. W. McCallum** *and* **V. Colapinto**, *both of St. Michael's Hospital, Toronto, Ontario, Canada.* Pre- and postoperative radiological urethrographic examinations and the surgical repair of membranous urethral structures are detailed in this book. Numerous radiological procedures are outlined describing the examination of the lower urinary tract. The literature is reviewed in detail with over 330 references and over 250 original radiographs and illustrations. A description of the neurogenic bladder is provided and a new method of radiological examination of the lower urinary tract in paraplegics is described. *'76, 377 pp. (6 3/4 x 9 3/4), 248 il., 2 tables, $35.50*

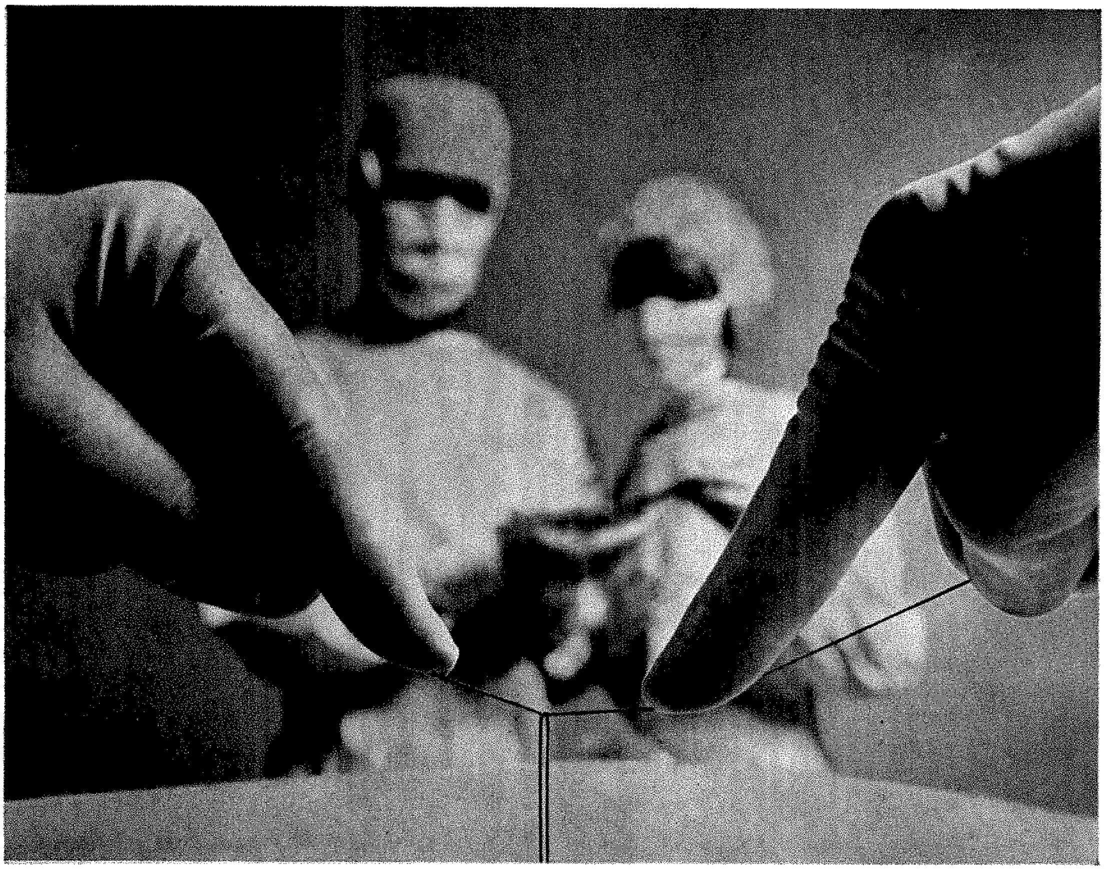
THE SYSTEMIC MANIFESTATIONS OF INFLAMMATORY BOWEL DISEASE *edited by* **William M. Lukash** *and* **Raymond B. Johnson**, *both of the National Naval Medical Center, Bethesda, Maryland. (30 Contributors)* The etiology and epidemiology of inflammatory bowel disease are covered with emphasis on numerous systemic manifestations, including the intestinal complications of toxic megacolon and malignancy and the extraintestinal manifestations of liver disease, skin involvement, ocular complications, arthritis, metabolic-endocrine implications, hematologic sequelae and urological complications. *'75, 368 pp., 92 il. (3 in color), 26 tables, $15.50*

NORMAL AND ABNORMAL GROWTH OF THE PROSTATE *edited by* **Martin Goland**, *Southwest Foundation for Research and Education, San Antonio, Texas. (90 Contributors)* This text covers such areas as embryology, development and pathology of the prostate gland, metabolism of steroids in prostatic tissue, regulation of prostatic metabolism, ligandmacromolecular binding and transport mechanisms, and experimental and clinical approaches to the prostatic cavity. *'75, 964 pp., 451 il., 123 tables, $48.75*

Orders with remittance sent by air, postpaid

301-327 East Lawrence Avenue • Springfield • Illinois • 62717 • USA

Monofilament Smooth



Because of the even diameter of ETHICON* Surgical Gut along its entire length, the smooth monofilament surface finish makes passage through tissue easier and smoother and produces less trauma.

Catgut beds down smoothly and securely with even the first throw of the knot and holds securely and strongly with standard surgical knots.

But we're not stopping there. Through research and development we continually strive to offer you, the surgeon, the finest absorbable suture available—but that's only some of the reasons why ETHICON surgical gut is today's most widely used suture material.

Catgut places a world of experience at your fingertips.

ETHICON
Trademark

When the difference is between being sure and being absolutely certain.

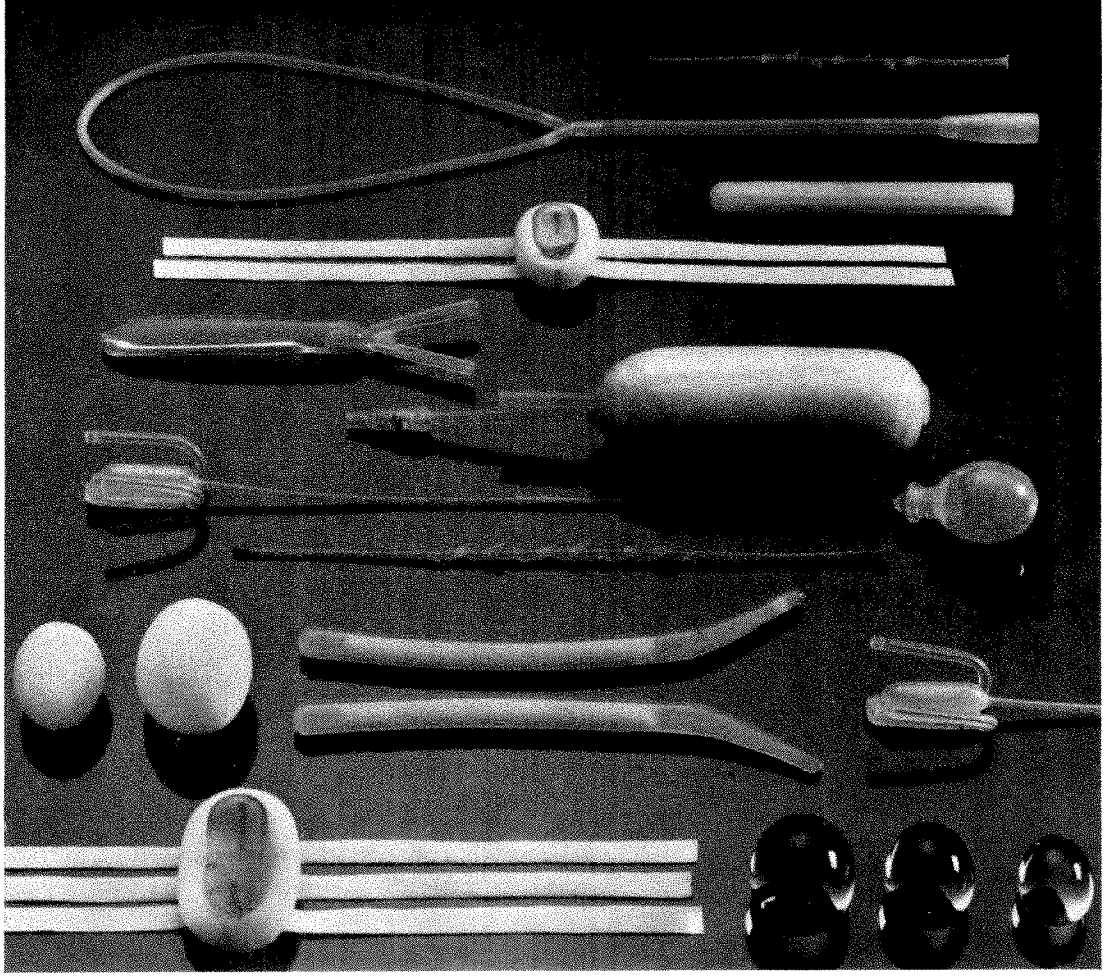
PLR 0508/5002

© ETHICON Ltd 1976 *Trademark

HEYER-SCHULTE

Complete range of
Silicone Implants for Urology

- Ureteral Stents
- Circle Nephro-Ureterostomy Tubes
- Penile Prostheses
- Vaginal Stents
- Testicular Prostheses
- Incontinence Prostheses



Full range available from

HEYER-SCHULTE

American Hospital Supply (U.K.) Limited

STATION ROAD, DIDCOT, OXFORDSHIRE OX11 7NP ENGLAND
TELEPHONE: DIDCOT (STD 0235) 814107 TELEX: 837127

British Journal of Urology (1976), **48**, 393-398 ©

The Ask-Upmark Kidney: A Form of Ascending Pyelonephritis ?

J. H. JOHNSTON and L. W. MIX
Alder Hey Children's Hospital, Eaton Road, Liverpool 12

In 1929, Ask-Upmark described a type of atrophic nephrosclerosis associated with arterial hypertension. The condition is characterised by a small kidney with 1 or more deep transverse grooves on the lateral convexity. Underlying the groove, the renal cortex is thin and scarred and the related calyx is dilated and clubbed, with an elongated infundibulum.

Following the original description, the lesion has become increasingly recognised as a cause of hypertension, particularly in young females, and has now acquired the status of being considered an eponymous clinico-pathological entity. Most authors on the subject have accepted the original contention of Ask-Upmark that the condition is of congenital, developmental origin. In our experience, the typical lesion, associated with hypertension, has been found in children with urinary infection and vesico-ureteric reflux. One such case is of particular interest in the context of the pathogenesis of the Ask-Upmark kidney since it clearly demonstrates that the lesion may be acquired and, further, that the onset of hypertension may be significantly delayed after the pathological changes are fully developed.

Case Report

B. E., 244085, first attended hospital at the age of 5½ years with a history of recurrent episodes of pyrexia and lethargy. She was found to have an *E. coli* urinary tract infection. Intravenous pyelography showed a normal upper tract bilaterally (Fig. 1). A urinary antiseptic was prescribed. No further urological investigation was undertaken nor was the blood pressure recorded.

4 years later the child was again referred to hospital, this time because of the recent onset of enuresis. Her urine again grew *E. coli* in significant numbers. A repeat intravenous pyelogram now showed that the right kidney was hypertrophied and of normal architecture; the left kidney was small, with thinning of the parenchyma over the convexity and clubbing and approximation of the calyces (Fig. 2). Micturating cystography revealed a sacculated bladder and left vesico-ureteric reflux (Fig. 3). The blood pressure was 100/70 mm Hg. Left ureteric reimplantation was performed to cure the reflux.

1 year following surgery, the child was well and her blood pressure was 120/80 mm Hg. Excretory urography showed no change in the state of the kidneys or the upper tracts. 2 years postoperatively, although she remained asymptomatic, her blood pressure was found to range from 170/115 mm Hg to 180/120 mm Hg. Excretory urography showed no alteration except for more pronounced hypertrophy of the right kidney. The urine was sterile. The creatinine clearance was normal as was the 24-hour urinary excretion of catecholamines. The peripheral venous blood renin was 15 pcg/ml (normal adult level 5-35 pcg/ml). The right renal vein renin was 24 pcg/ml and the left 41 pcg/ml, a ratio of 1 to 1·7.

The hypertension proved to be refractory to medical management and 6 months after diagnosis, left nephrectomy was performed. The blood pressure returned to 120/80 mm Hg within 4 days of operation and has remained normal, without medication, for 2 years subsequently.

Pathology

The left kidney was small, measuring some 5 × 3 cm and demonstrated 2 deep transverse grooves on the lateral border near the kidney poles. Section showed that between each groove and the underlying dilated calyx, the parenchyma was thin (Fig. 4). Histologically, the scarred areas showed multiple thick-walled tortuous blood vessels, a few scarred glomeruli and atrophic tubules lined with a single layer of cuboidal cells and containing colloid material. There was some lymphocytic infiltration in the para-pelvic region. A sharp line of demarcation was present between the scarred areas and the adjacent normal renal tissue (Fig. 5).

UNIVERSITY COLLEGE OF MEDICINE LIBRARY C. U.

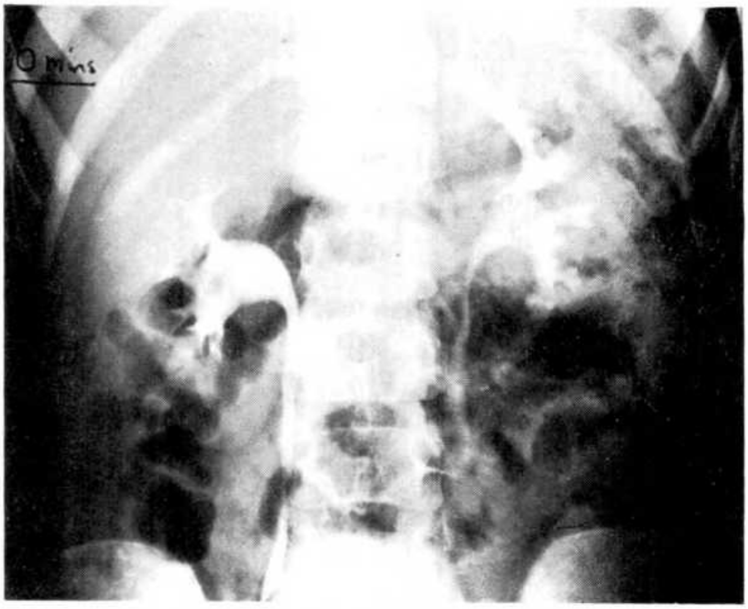


Fig. 1. Intravenous pyelogram aged 5½ years showing normal kidneys.

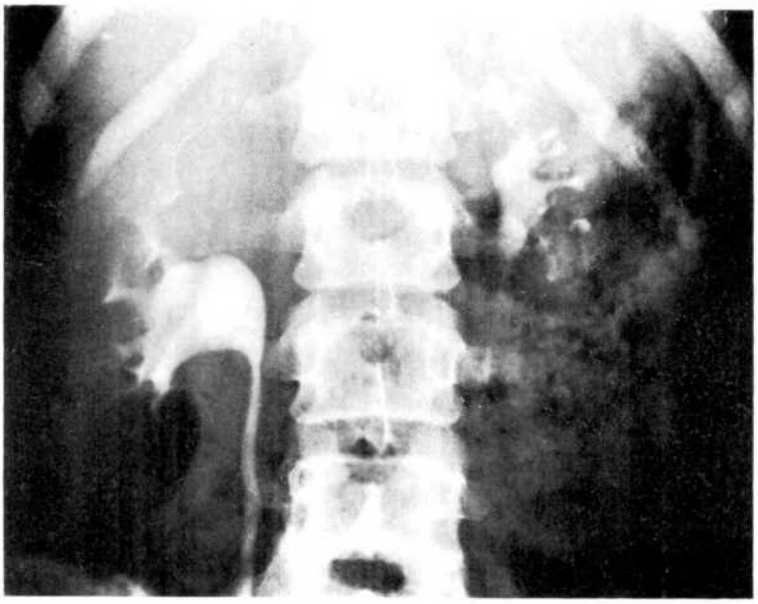


Fig. 2. Intravenous pyelogram aged 9 years. Right kidney hypertrophied. Left kidney small, with thin parenchyma and approximation and clubbing of calyces.

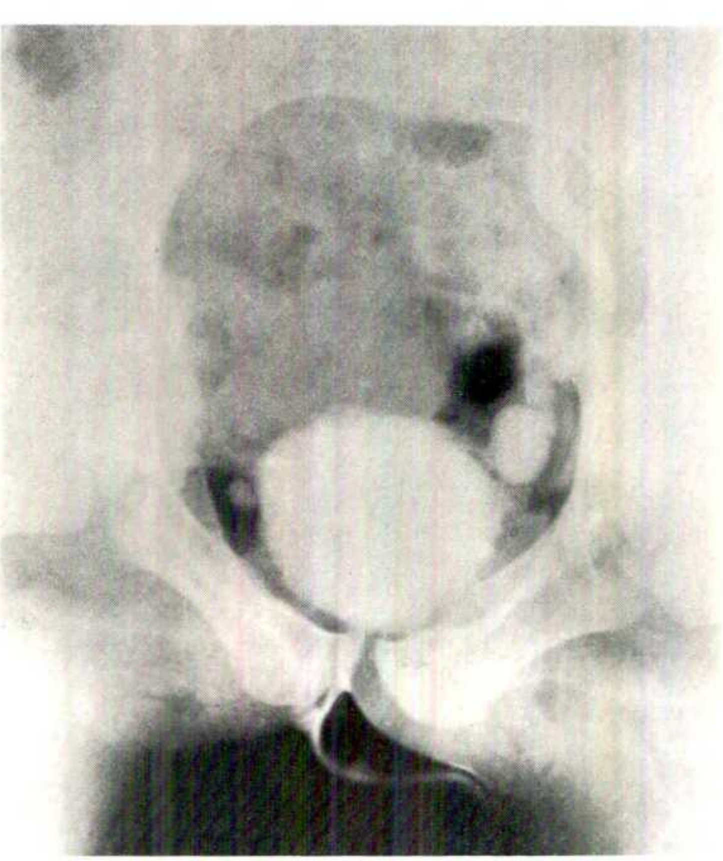


Fig. 3. Micturating cystogram showing sacculated bladder and left vesico-ureteric reflux.

Discussion

The Ask-Upmark kidney has typically been encountered in hypertensive female children (Himmelfarb *et al.*, 1975). Kaufman and Fay (1974) found the female to male ratio to be 6·7 to 1. Most commonly only 1 kidney is affected but the condition may be bilateral. The kidney is small and may contain 1 or several segmental scars. In the scarred area, glomeruli are either entirely absent or are few in number and fibrotic or hyalinised. The tubules are atrophic and either small or distended with colloid to produce a pseudo-thyroid appearance. The arterioles are classically thick walled, close together and tortuous. There is little or no inflammatory cell infiltration. The renal parenchyma outside the affected segment is usually histologically normal although there may be sclerotic changes secondary to long standing hypertension (Royer, 1968). In all cases reported prior to the present one, hypertension was present at the time of diagnosis of the renal pathology. The hypertension is due to increased renin production (Fikri, Haarahan and Stept, 1973; Rosenfeld *et al.*, 1973; Kaufman and Fay, 1974). Meares and Gross (1972) have demonstrated diffuse hyperplasia of the juxta-glomerular cells in the normal renal cortex. The prognosis depends upon the extent of the disease and the duration of hypertension (Himmelfarb *et al.*, 1975). The condition is potentially curable by nephrectomy when the disease is unilateral.

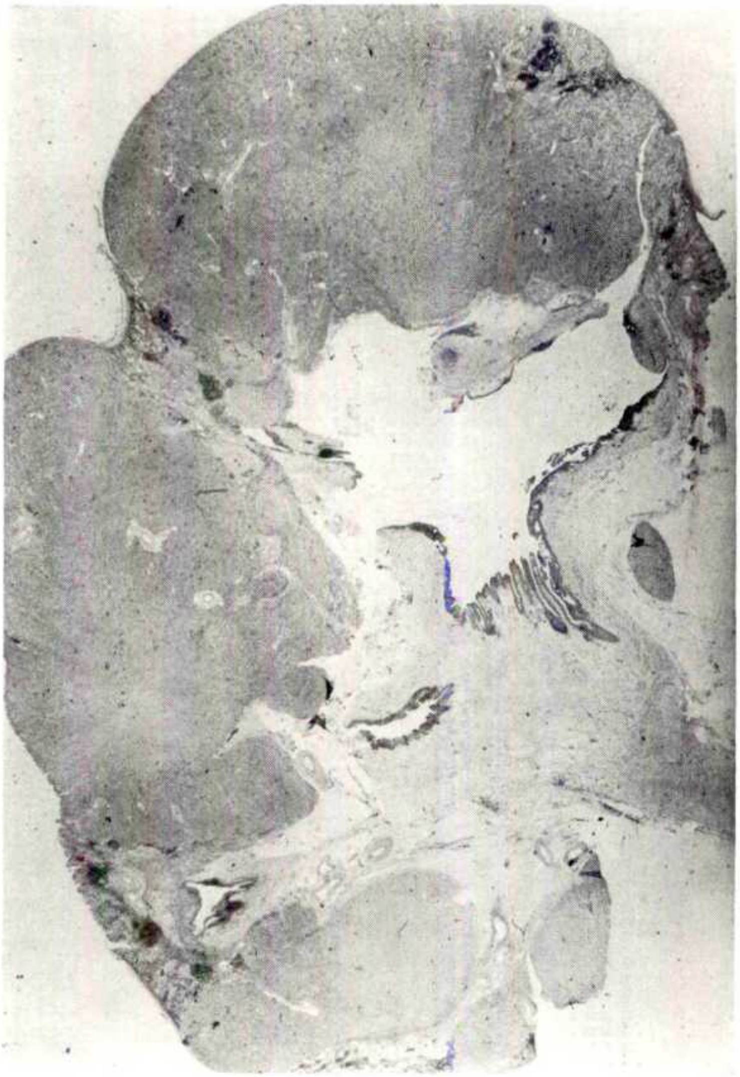


Fig. 4. Vertical section through nephrectomy specimen showing localised deep scars on the convexity involving the entire thickness of the parenchyma.

The pathogenesis of the Ask-Upmark kidney has remained uncertain and a matter of conjecture. The original author postulated a congenital segmental hypoplasia and Hayman (1971) was of the same opinion, believing that nephrogenesis had been arrested in one or more reniculi. Kaufman and Fay (1974) thought that localised ischaemic damage was inflicted on the kidney about the 10th week of intra-uterine life. However, Ljungqvist and Lagergren (1962) showed, from microangiographic studies, that there is blood flow into the involved segment. These authors considered the scarred area to represent the juxta-medullary cortex which is particularly susceptible to hypoxia in early life.

The histological changes of chronic pyelonephritic atrophy are identical with those described for the scarred areas in the Ask-Upmark kidney (Harrison, 1972). In the patient of Dein *et al.*

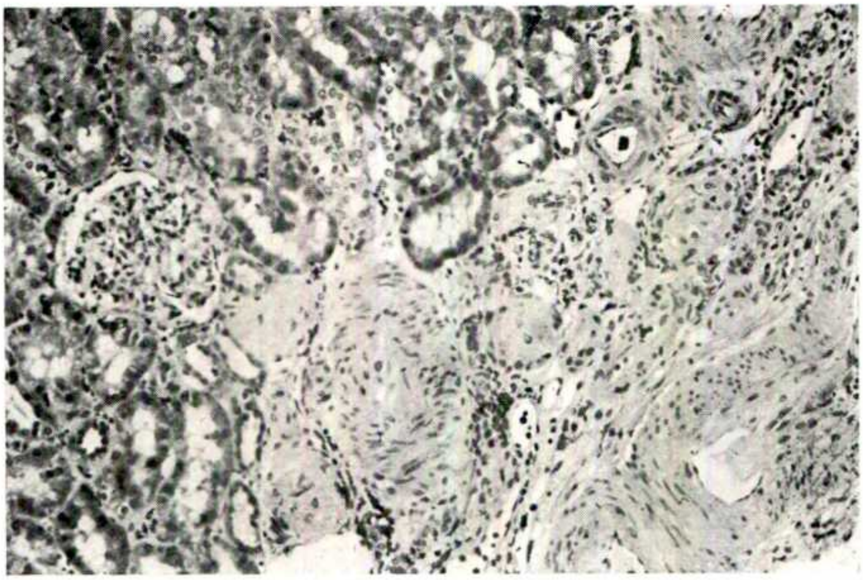


Fig. 5. Histology (× 50) showing sharp line of demarcation between scarred and normal kidney tissue. Scarred area contains tortuous, thick-walled blood vessels and some tubules.

(1973), as in the present case, there were urinary tract infection and vesico-ureteric reflux to the affected kidney suggesting that the renal changes may be the result of ascending pyelonephritis. In our patient, this concept receives further support from the fact that the kidney was radiologically normal 4 years before the scarring was seen.

Rolleston, Maling and Hodson (1974) have shown that in children, pyelo-tubular reflux produces scarring restricted to the areas into which the reflux occurred. Hodson (1974) demonstrated the same phenomenon in young pigs and noted that the parenchymal changes may occur even when the urine is sterile.

Unfortunately, cystography was not performed in our patient at the time of first presentation but the pathological anatomy of the Ask-Upmark kidney suggests that localised calyco-tubular reflux could have been responsible for the characteristic features. In our experience, hypertension is a rare complication of the unilateral scarred pyelonephritic kidney associated with vesico-ureteric reflux. The reason why it develops in some children and not in others remains obscure. However, the present case indicates that children with severe unilateral renal damage require a lengthy follow-up and regular blood pressure measurements.

Summary

The case is presented of a young girl with recurrent urinary tract infection and vesico-ureteric reflux who developed a small scarred kidney and subsequently, hypertension. Pathologically, the renal changes were compatible with those of an Ask-Upmark kidney.

The pathogenesis of the Ask-Upmark kidney is discussed.

It is postulated that the lesion is not necessarily of congenital origin but may well be related to infection and intra-renal reflux.

It is concluded that long-term follow-up of a young patient with a scarred kidney is indicated.

References

Ask-Upmark, E. (1929). Über juvenile maligne Nephrosklerose und ihr Verhältnis zu Störungen in der Nierenentwicklung. *Acta Pathologica et Microbiologica Scandinavica*, **6**, 383-442.

Dein, T. W., Walker, D. and Hackett, R. L. (1973). The Ask-Upmark kidney: a case report. *Archives of Pathology*, **96**, 10-13.

Fikri, E., Hanrahan, J. B. and Stept, L. A. (1973). Renovascular hypertension in a child: Ask-Upmark kidney. *Journal of Urology*, **110**, 728-731.

Harrison, A. R. (1972). Pyelonephritis. In *Modern Trends in Urology*—3, ed. Sir Eric Riches. London: Butterworths, pp. 3-17.

Hayman, J. M. (1971). Congenital malformations of the kidney. In: *Diseases of the Kidney*, 2nd ed., Vol. 2, Ed. M. B. Strauss and L. G. Welt. Boston: Little, Brown and Co., pp. 1297-1307.

Himmelfarb, E., Rabinowitz, J. G., Parve, L., Gammill, S. and Arant, B. (1975). The Ask-Upmark kidney; roentgenographic and pathological features. *American Journal of Diseases of Children*, **129**, 1440-1444.

Hodson, C. J. (1974). Vesico-ureteric reflux and renal scarring with and without infection. In: *Proceedings of the Fifth International Congress of Nephrology, Mexico 1972*, ed. H. Villarreal. New York: Karger. Abstract page 598.

Kaufman, J. and Fay, R. (1974). Renal hypertension in children. In: *Reviews in Paediatric Urology*, ed. J. H. Johnston and W. E. Goodwin. Amsterdam: Excerpta Medica, pp. 201-240.

Ljungqvist, A. and Lagergren, C. (1962). The Ask-Upmark kidney: a congenital renal anomaly studied by micro-angiography and histology. *Acta Pathologica et Microbiologica Scandinavica*, **56**, 277-283.

Meares, E. M. and Gross, D. M. (1972). Hypertension owing to unilateral renal hypoplasia. *Journal of Urology*, **108**, 197-201.

Rolleston, G. L., Maling, T. M. and Hodson, C. J. (1974). Intrarenal reflux and the scarred kidney. *Archives of Disease in Childhood*, **49**, 531-539.

Rosenfield, J. B., Cohen, L., Garty, I. and Ben-Basset, M. (1973). Unilateral renal hypoplasia with hypertension (Ask-Upmark kidney). *British Medical Journal*, **2**, 217-218.

Royer, P. (1968). Renal hypoplasia. In: *Nephrology*, Vol. 2, ed. J. Hamburger (and others).. London: Saunders, pp. 1059-1069.

The Authors

J. H. Johnston, FRCS, FRCSI, Consultant Urological Surgeon.
L. W. Mix, MD, FRCS(C) Research Fellow in Paediatric Urology.

British Journal of Urology (1976), **48**, 399-401 ©

The Surgical Significance of the Proteus Stone

W. K. MOORES
The Liverpool Regional Urological Centre, Sefton General Hospital, Liverpool

In recent years, several technical aids to achieve complete stone clearance at operation have been advocated. The Gil Vernet pyelotomy (Gil Vernet, 1965) in which the renal pelvis is approached posteriorly and opened within the renal sinus, has gained wide acceptance. The use of preoperative contact X-rays, with a sterilisable X-ray cone, and the grid sling to localise residual stone fragments accurately, has been well described (Hanley, 1967). Wickham has devised a simple continuous irrigating system for washing stone fragments out of the kidney at operation (Hanley, 1970). Clamping the renal pedicle with kidney cooling to increase the ischaemia time (Wickham, Hanley and Joekes, 1967) allows a thorough search of the renal pelvis to be carried out in a dry field. The techniques of kidney cooling have undergone several improvements, and a recent method (Hanley, 1970) utilises nitrous oxide gas, which passes through coils applied to the kidney. The indications for the use of renal hypothermia are controversial, however, despite good reports of kidney clearance.

The natural history of recurrences following removal of stones due to the proteus organism is described. The results indicate that all aids to complete stone clearance are appropriate in the conservative surgery of the proteus stone.

Patients and Methods

62 patients with staghorn calculi who had undergone conservative surgery at the Liverpool Regional Urological Centre since 1962 were reviewed. The data obtained were recorded on an item-based card index system (J. L. Jolley and Partners Limited). The following classification of staghorn calculi was adopted:

Type A: Calculi occupying pelvis and passing into three major calyces.
Type B: Calculi occupying pelvis and passing into two major calyces.
Type C: Calculi occupying pelvis and passing into one major calyx.
Type D: Calculi forming a cast of a single calyx.
Type E: Calculi occupying the pelvis and extending into the necks of the calyces.
Type F: Calculi forming a mould of the lower moiety of a duplex kidney.

Findings

Incidence of Bilateral Calculi (see Table I)

36 patients had staghorn calculi with proteus infection. Of these, 22 (61 %) had either, at presentation or in the past, stones in the opposite kidney. 15 (42 %) of these stones were staghorn calculi.

26 patients had staghorn calculi which were not associated with the proteus organism. Of these, 12 (46 %) had had stones in the opposite kidney, of which 6 (23 %) were of a staghorn configuration.

These figures suggest that the proteus organism is more likely to cause bilateral calculi, and that if 1 of the stones has a staghorn configuration, the stone in the opposite kidney is very likely to be a staghorn calculus as well.

Table I
Incidence of Bilaterality

	Proteus (36 patients)	Non-proteus (26 patients)
Bilateral stones	22 (61%)	12 (46%)
Bilateral staghorn calculi	15 (42%)	6 (23%)

Table II
Size of Stone

Type	Proteus (48 operations)	Non-proteus (28 operations)
A	34 (71%)	16 (57%)
B	5	0
C	3	4
D	5	2
E	1	4
F	0	2

Size of Stone (see Table II)

39 out of 48 staghorn calculi due to proteus (81%) were either type A or type B, whereas 16 out of 28 (57%) non-proteus staghorn calculi in this series were of this size, *i.e.*, the proteus stones tend to be larger than other types of staghorn calculi.

Results of Surgery (see Table III)

The total recurrence rates for proteus and non-proteus stones in this series were 52% and 43% respectively. The incidence of true recurrence among the proteus stones, however, was 38%, against 16% for the non-proteus group, despite there being a surprisingly better clearance rate following operations for proteus stones. This evidence indicates that proteus stones have a greater tendency to recur after complete kidney clearance.

Behaviour of Recurrences (see Table IV)

There were 25 recurrences following conservative operations for proteus stones in this series. 11 (44%) of these re-enlarged to a staghorn configuration, of which 8 were complete type A stones, and 3 incomplete. 8 of these kidneys required further surgery, and 5 (20%) were removed.

Amongst 12 kidneys which contained recurrent stone, in which the original stone was not due to proteus, no stone enlarged to a staghorn shape or size. 4 further operations for stone were necessary in this group, 2 ureterolithotomies, 1 pyelolithotomy, and 1 (8%) nephrectomy.

From this evidence, recurrences due to proteus tend to enlarge and lead to a high rate of nephrectomy. Recurrent stones due to other organisms, however, have a tendency to remain small and not to give rise to complications.

It should be stressed that these results have been collected from cases treated over the last 14 years, and that the value of complete stone clearance and close follow-up supervision has been fully appreciated only in recent years.

Discussion

The evidence in this series shows that staghorn calculi due to the proteus organism tend to be bilateral more often; to be larger; to recur more often after surgery; and to result in secondary nephrectomy more often, than staghorn calculi due to other organisms. This confirms the finding of King and Boyce (1963) that stone accretion *in vitro* occurs most rapidly in the presence of the proteus organism.

Wickham and Mathur (1971) demonstrated that they were able to reduce the rate of incomplete removal of staghorn calculi from 60% to 0% using local circulatory arrest with kidney cooling. Furthermore, they showed that the true recurrence rate fell from 64% to 4% when complete kidney clearance had been achieved. Singh, Tresidder and Blandy (1971), however, say that a prolonged search for small stone particles would lead to an unacceptable reduction of kidney

Table III

Results of Surgery

	Proteus (48 operations)	Non-proteus (28 operations)
Incomplete removal	11 (23%)	9 (32%)
True recurrence	14/37 (38%)	3/17 (16%)
Total recurrence	25 (52%)	12 (43%)

Table IV

Behaviour of Recurrent Stones

	Proteus (48 operations)	Non-proteus (28 operations)
Total recurrence	25	12
Recurrence to staghorn	11 (44%)	0
Total	8	—
Partial	3	—
Further stone surgery same kidney	8/48 (17%)	3/28 (11%)
Nephrectomy	5/48 (10%)	1/28 (4%)

function with minimal benefit to the patient. They described the relatively benign behaviour of their incompletely removed stones and they think that to leave particles of stone behind is not the disaster which is sometimes believed. They, therefore, do not advocate the routine use of renal hypothermia and believe it is only necessary where the pelvis is intrarenal, and the parenchyma is well preserved, when delivery of the stone would be difficult.

However, neither Wickham and Mathur nor Singh *et al.* related the behaviour of their recurrences to the causative organism. The evidence of this review indicates that stone disease and the behaviour of recurrent stone due to proteus is a far more aggressive process than that due to other organisms. All aids to complete stone clearance including local circulatory arrest would seem appropriate to achieve complete clearance of stone at operation.

Summary

62 patients with staghorn calculi who underwent conservative surgery at the Liverpool Regional Urological Centre since 1962 have been reviewed.

The evidence shows that stone disease due to proteus is more rapidly progressive than that due to other organisms. Recurrences of proteus stones continue to behave in the same manner. Complete kidney clearance at operation is an essential part of the management of these stones, if renal substance is to be preserved.

The author is grateful to Mr N. O. K. Gibbon, Mr R. M. Jameson, and Mr J. G. Gow for allowing him to study their cases, and also to Mr P. J. O'Boyle for many helpful criticisms.

References

Gil Vernet, J. (1965). New surgical concepts in removing renal calculi. *Urologia Internationalis*, **20**, 255-288.

Hanley, H. G. (1967). Accurate surgical localisation of renal calculi. *British Journal of Urology*, **39**, 159-161.

Hanley, H. G. (1970). An improved system of local renal hypothermia with special reference to the pseudo-recurrence rate of staghorn calculi. *British Journal of Urology*, **42**, 540-544.

King, J. S. and Boyce, W. H. (1963). *In vitro* production of simulated renal calculi. *Journal of Urology*, **89**, 546-551.

Singh, M., Tresidder, G. C. and Blandy, J. (1971). The long term results of removal of staghorn calculi by extended pyelolithotomy without cooling or renal artery occlusion. *British Journal of Urology*, **43**, 658-664.

Wickham, J. E. A., Hanley, H. G., and Joekes, A. M., (1967). Regional renal hypothermia. *British Journal of Urology*, **39**, 727-743.

Wickham, J. E. A., and Mathur, V. K., (1971). Hypothermia in the conservative surgery of renal disease. *British Journal of Urology*, **43**, 648-657.

The Author

W. K. Moores, FRCS, Urological Registrar.

British Journal of Urology (1976), **48**, 402 ©

Short Case Report

Contralateral Ureteric Metastasis from Renal Carcinoma

A woman, 55, complained of haematuria and left loin pain for 6 months. No abnormality could be found on clinical examination. An IVP showed a non-functioning right kidney and a space-occupying lesion in the lower pole of the left. Ascending ureterography demonstrated a filling defect, obstructing the right ureter at the level of L4-5 (Fig.) and a distorted pelvi-calyceal system in the lower pole of the left kidney. Selective renal arteriography confirmed the diagnosis of left renal tumour.

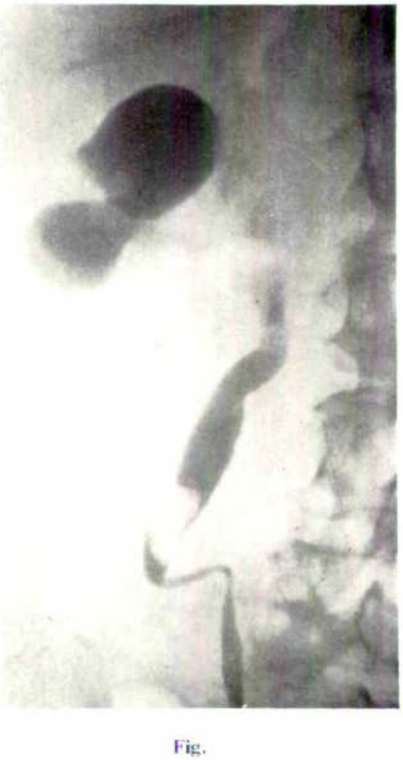


Fig.

The right ureter was explored first and a smooth, 2-cm-long polypoid lesion was resected and end-to-end anastomosis of the ureter performed. Histology showed a secondary clear cell tumour consistent with a renal primary. Her postoperative recovery was uncomplicated.

After convalescence a repeat IVP showed very poor function of the right kidney. A right ureteric catheter collection of urine showed very poor renal function.

The left kidney was explored and a 5 cm lower pole clear cell carcinoma was removed by a $\frac{3}{5}$th partial nephrectomy.

Postoperatively her blood urea rose to a peak of 15·6 mmol/l. but fell to 12·6 mmol/l. by discharge. She remains well at 3 months.

Comment

Metastases from renal cell carcinoma are rarely found in the ureter, especially the contralateral one. The presence of a ureteric secondary from a renal carcinoma is usually indicative of generalised metastatic disease (Gross and Minkowitz, 1971).

M. A. HUGHES, D. G. ARKELL, P. DAWSON-EDWARDS and J. R. GEDDES

Dept. of Urology, Queen Elizabeth Hospital, Birmingham

Reference

GROSS M. and MINKOWITZ S. (1971). Ureteral metastasis from renal adenocarcinoma. *Journal of Urology*, **106**, 23-26.

British Journal of Urology (1976), **48**, 403-412 ©

The Thermogravimetric Analysis of Renal Stones (in clinical practice)

G. ALAN ROSE and C. WOODFINE
St Peter's Hospitals and Institute of Urology, London

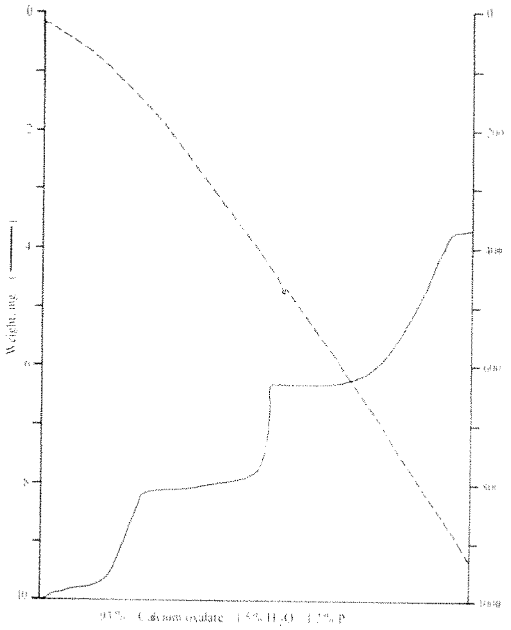
Analysis of renal calculi continues to be poorly performed in most hospital laboratories. With a few notable exceptions, analysis is usually qualitative and schemes of quantitative chemical analysis, as suggested by Hodgkinson, Peacock and Nicholson (1969) and by Westbury and Omenogor (1970), do not seem to have been widely adopted. At best, chemical methods can indicate only the radicals that are present and not the actual compounds. By contrast, physical methods hold out the possibility of identification of compounds themselves. X-ray crystallography has been extensively used for stone analysis (Tsay, 1961; Herring, 1962; Sutor and Scheidt, 1968; Bellanato *et al.*, 1973) and infra-red spectroscopy has been popular in certain centres. Both these methods, however, are not fully quantitative.

As long ago as 1966, Strates suggested that a thermogravimetric (TG) technique lent itself to the analysis of renal calculi. In this technique, a substance is heated gradually and linearly while on a balance to a high temperature (often 1,000°C) and the weight changes occurring at particular temperatures observed. Certain chemicals lose weight at specific temperatures so permitting their characterisation. The particular temperatures at which the weight changes occur indicate the nature of the chemical present and the extents of the changes indicate the amounts present. Hence TG analysis offers the prospect of identifying compounds present both fully and quantitatively.

Thermoanalytic data for common types of renal calculi were given by Strates and Georgacopoulou (1969) and by Berenyi and Liptay (1971) who recommended TG analysis for renal calculi. Nevertheless, use of the method has not been widely adopted and we are unaware of any report describing an extensive use of TG analysis of renal calculi. Suitable TG analysis equipment was aquired by the Institute of Urology in 1972 and has been used in these hospitals for routine analysis of renal calculi since then. This report describes our experiences in this field and indicates the advantages and disadvantages of analysing renal calculi in this way.

Method

The TG equipment was a Stanton Redcroft thermo balance TG 750 (Coppermill Lane, London SW17 0BW) in conjunction with a twin pen X1, X2 recorder to indicate temperature and weight respectively. A consecutive series of 502 renal calculi was subjected to analysis whenever possible. Each calculus was cleansed of blood and tissue, air dried, divided into representative portions where appropriate and then crushed. Usually 10 mg of crushed material was used for TG analysis but sometimes this was reduced to 5 mg or less. Occasionally as little as 1 mg was used. The temperature rise was set to 30°C per min and the final temperature for each run was 1,000°C. Whilst in operation, the furnace was supplied with cold running water; unfortunately problems with an unstable water supply caused the destruction of 2 furnaces before an automatic cut-out device (Flowtrol, from Edwards High Vacuum Co. Ltd, Crawley, Surrey) was fitted. Subsequently models of the equipment were fitted with an electronic cut-out to avoid this hazard. Experiments showed that sharper weight changes were obtained with an atmosphere of flowing oxygen and this gas was therefore used at a flow rate of about 30 ml/min. Each renal calculus was also analysed chemically by the quantitative method of Westbury and Omenogor (1970) as modified by Westbury (1974) provided that there was sufficient material. Occasionally there was only sufficient for TG analysis alone.



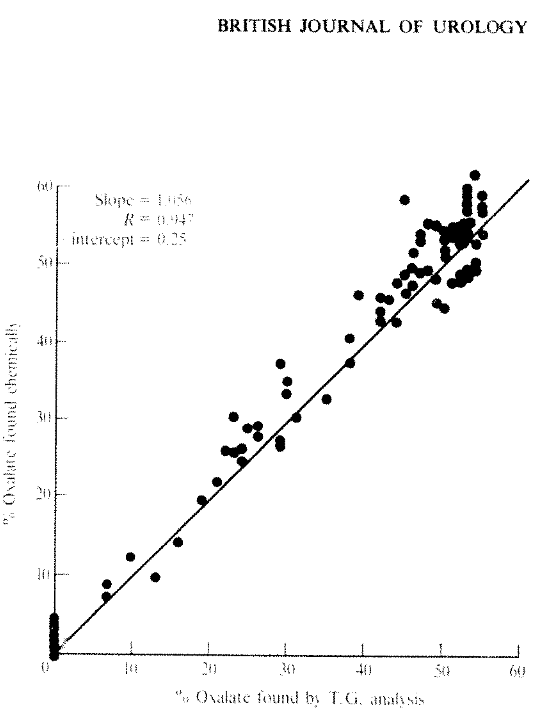


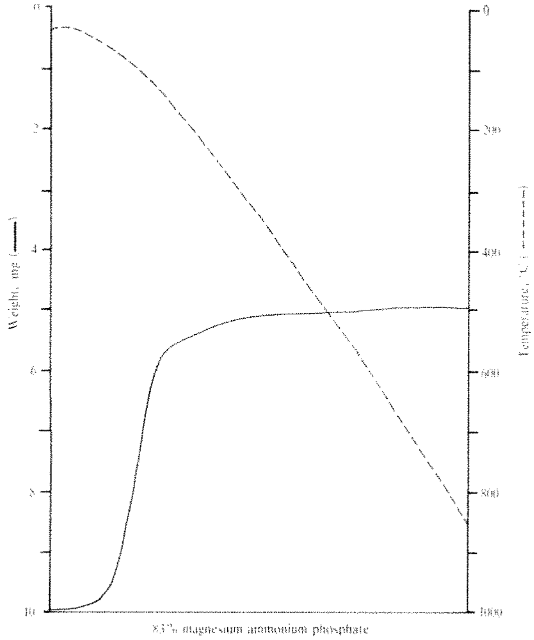
Fig. 1 (left). TG tracing from a renal calculus which was 93% calcium oxalate, 1·5 H_2O and 1·2 phosphorus. (For explanation see text.)

Fig. 2 (right). Comparison of oxalate content of renal calculi as found by chemical and TG analytical methods. The line is not a regression curve but the line of complete identity. The regression line is given by $y = 1{\cdot}056x + 0{\cdot}25$; $R = 0{\cdot}947$.

Results

Most of the calculi proved to have TG tracings which readily permitted identification with known pure compounds. Figure 1 shows the tracing obtained in the case of a stone which proved chemically to contain 93% calcium oxalate and 1·2% phosphorus. Several points should be noted in this tracing. The first small weight loss of about 0·2 mg is presumably due to loss of loosely bound water. The first major weight loss occurring at about 100°C is due to loss of water of crystallisation and from the ratio of this weight of water to the weight of oxalate (see below) the degree of hydration of the calcium oxalate can be calculated to be 1·5 molecules of H_2O per molecule of calcium oxalate. The next rather small weight loss of about 0·2 mg (150° to 350°C) is probably due to destruction of stone matrix. Reference to Figure 7, however, will show that traces of urate would be included at the end of this temperature section. The next sharp weight change at about 400°C is due to the loss of carbon monoxide which converts calcium oxalate to calcium carbonate. This reaction is exothermic, so accounting for the spike in the temperature curve. Finally, the loss of weight at about 500° to 900° is due to loss of carbon dioxide converting calcium carbonate to calcium oxide. The oxalate can be calculated from either the CO weight loss at 400°C or the later CO_2 loss. The ratio of these weight losses should always be the same for pure calcium oxalate and any excess CO_2 loss not explained by a corresponding CO loss, must be due to calcium carbonate having being present in the original calculus. The correlation between oxalate found chemically and by TG analysis for those cases in which this substance was identified is shown in Figure 2.

In the case of stones containing calcium oxalate, the TG tracing invariably shows weight loss at about 100°C and due to loss of water of crystallisation. This is because the solid phase of calcium oxalate occurs as the monohydrate or the dihydrate but apparently not in urine as the



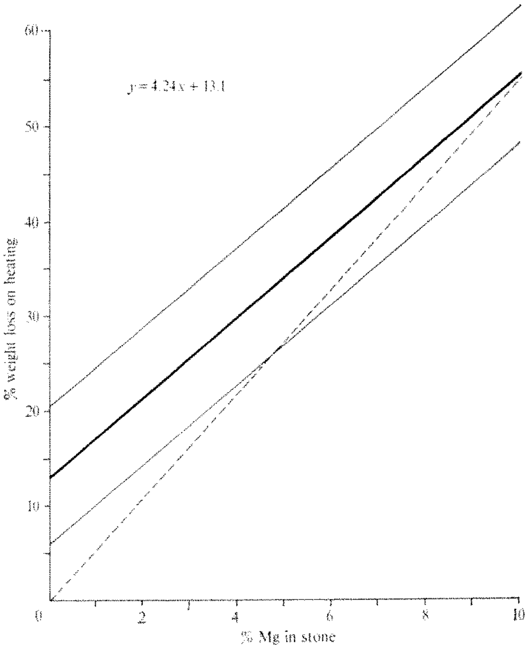


Fig. 3 (left). TG tracing from a renal calculus which was found chemically to contain 83% magnesium ammonium phosphate. (For explanation see text.)

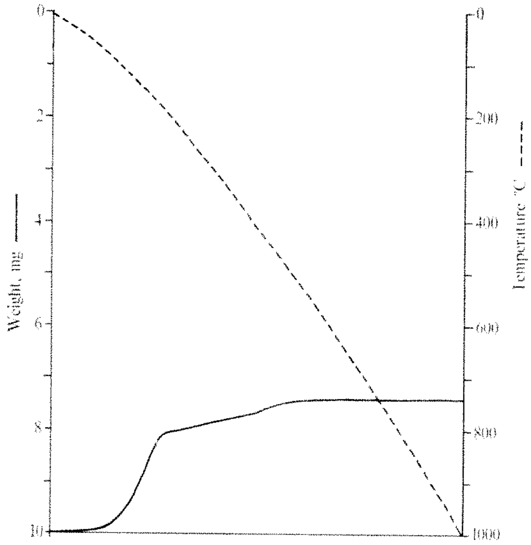
Fig. 4 (right). Comparison in 140 renal calculi of magnesium found chemically and the total weight loss on heating. The thick regression line is given by the equation $y = 4{\cdot}24x + 13{\cdot}1$; ($R = 0{\cdot}80$); the thin continuous lines indicate standard error of estimate; the thin dotted line indicates equivalence between magnesium and weight loss due to magnesium ammonium phosphate.

anhydrous form. The proportion of the 2 forms that are present can be readily calculated. Thus, if the hydrate, calculated as shown above, appears to be 1·4, there must be present 60% of monohydrate and 40% of the dihydrate. The presence of Brushite in large amounts would render this calculation invalid, since the loss of water could then not be assigned accurately to the oxalate. Fortunately, however, the presence of Brushite in oxalate stones is unusual (see below) and the arbitrary assumption has been made that the calculation of degree of hydration of oxalate is valid, provided that the stone is over 70% calcium oxalate. It is therefore unlikely that there can be large errors in results presented.

Figure 3 shows the TG tracing obtained from a stone which was found chemically to contain 83% magnesium ammonium phosphate. Note the early loss of weight at about 100°C with very little change above 200°C. This weight loss is due to loss of 6 moles of water and 1 of ammonia to yield $MgHPO_4$.

Figure 4 shows the correlation between magnesium found chemically and percentage of weight loss in those stones showing a tracing compatible with magnesium ammonium phosphate.

Figure 5 shows the TG tracing from a stone which was found chemically to be calcium phosphate with a Ca/P ratio compatible with Brushite. This is confirmed by the TG tracing which shows loss of water of crystallisation compatible with the formula $CaHPO_4.2H_2O$. Note the similarity between Figures 3 and 5. A consecutive series of 100 calculi, each of which was found by chemical analysis to contain more than 50% magnesium ammonium phosphate, was studied to see what other ingredients accompanied the triple phosphate. Only 3 stones proved to be pure magnesium ammonium phosphate but calcium phosphate was the only other ingredient in 92



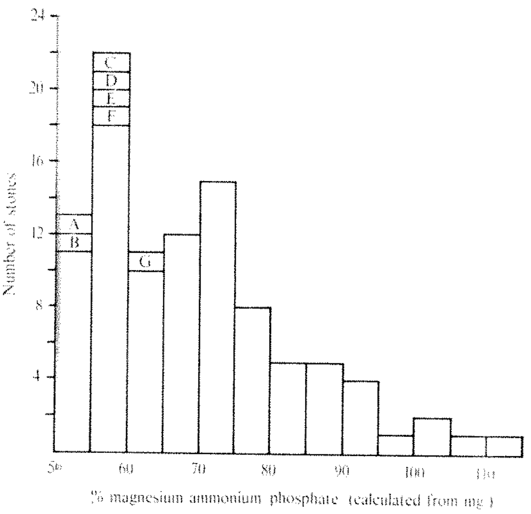


Fig. 5 (left). TG tracing from a renal calculus which was found to contain Brushite ($CaHPO_4 . 2H_2O$) as the only mineral. Note that although superficially similar to Figure 3 there are differences. With Brushite the weight loss commences at a higher temperature, occurs over a shorter temperature range and is greater than for Struvite.

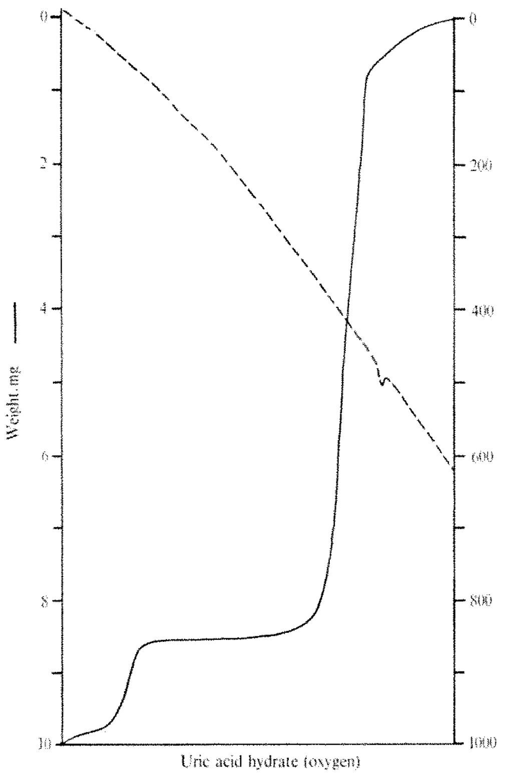
Fig. 6 (right). The composition of 100 renal calculi each of which contained more than 50% magnesium ammonium phosphate as found chemically. The only other ingredient was calcium phosphate except in 7 stones identified by the following letters A, 8·8% uric acid; B, 26% uric acid and 9% oxalate (this stone had formed on a suture); C, 7·3% uric acid; D, 6% oxalate; E, 11% oxalate; F, 13% oxalate (this stone formed on hair of skin transplanted into the renal tract); G, 8% uric acid. Thus pure Struvite stones are uncommon, this mineral usually being accompanied by calcium phosphates.

stones; a further 2 contained over 5% uric acid and magnesium ammonium phosphate and the remaining 3 contained over 5% oxalate plus calcium phosphate. The composition of these 100 calculi are illustrated in Figure 6.

Figure 7 shows the TG tracing from a stone which was found chemically to be 89% uric acid. The main weight loss is at about 450°C, although there is some tailing off which continues until about 600°C. Nevertheless, the tracing is readily identifiable and the percentage of uric acid can be calculated with reasonable accuracy. The weight loss at about 100°C was due to water of crystallisation, an unusual finding in uric acid calculi in our experience. A similar tracing would have been given by ammonium urate, and the detection of the ammonia would have depended upon the chemical analysis. The correlation between uric acid found by TG analysis and by chemical method is shown in Figure 8.

Figure 9 shows the TG tracings in atmospheres of air and oxygen respectively from a stone which was found by qualitative analysis to contain only cystine. Note that in oxygen most of the weight loss takes place fairly sharply at about 200°C, so giving a characteristic tracing and that weight loss is virtually complete. Using an atmosphere of air, the weight loss extends over a greater range of temperature. Regardless of which atmosphere is used, a characteristic odour is released which itself indicates the nature of the compound, although of course not quantitatively.

Table I shows the result of TG analysis of 502 consecutive renal calculi. 63% could have been completely and quantitatively identified by TG analysis alone. TG analysis gave useful qualitative information in a further 31% but was unhelpful in about 6%.



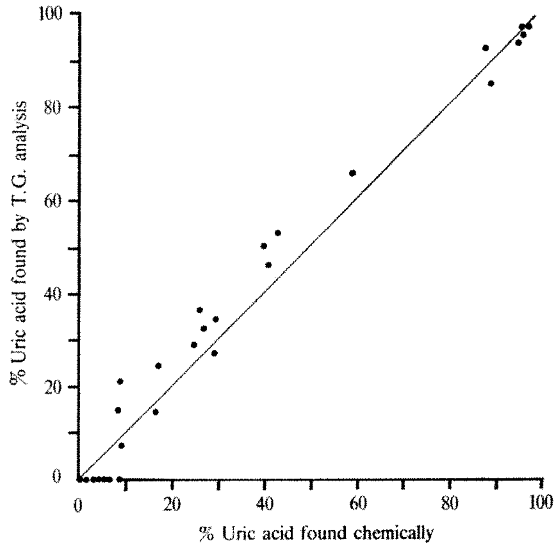


Fig. 7 (left). TG tracing from a renal calculus which was found chemically to contain 89% uric acid. No minerals or ammonia were detected and the stone must have been the monohydrate. (See text.)

Fig. 8 (right). Comparison of uric acid content of 27 renal calculi found by chemical and TG analytical methods and which contained measurable quantities of this chemical. The thin line shows complete correspondence (45° slope). The regression line is given by the equation $y = 0{\cdot}97x + 0{\cdot}04$.

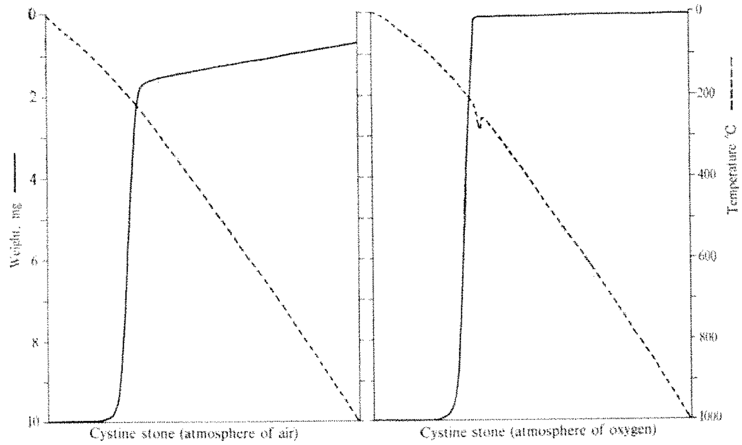


Fig. 9. TG tracings from a renal calculus made virtually of cystine alone and using atmospheres of flowing air (left) and oxygen (right).

Table I

Thermogravimetric Analyses of 502 Renal Calculii

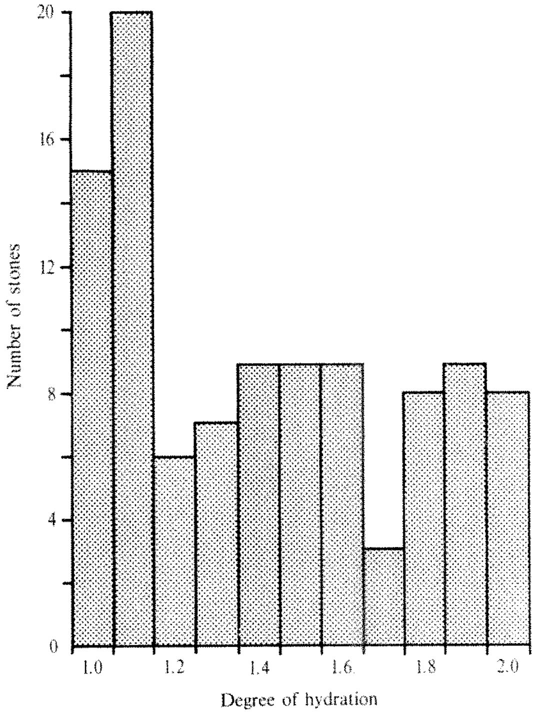
	No.	%
Successful		
Pure calcium oxalate	110	21·9
Calcium oxalate/phosphate	170	33·9
Uric/ammonium urate	16	3·2
Calcium oxalate/urate	14	2·8
Cystine	5	1·0
	315	62·8
Less Successful		
Mag. ammon. phos/Ca phos.	135	26·9
MAP/Ca phos/& other traces	22	4·4
	157	31·3
Failures		
Other complex mixtures	30	6·0
	502	101

Figure 10 shows the calculated degree of hydration in each of a series of renal calculi, each of which was found to contain over 70% of calcium oxalate. There were 10 renal calculi in this series in which it was possible to separate inside and outside portions for separate TG analysis and in which a content of calcium oxalate was over 70% in both portions. The degrees of hydration revealed by TG analysis of these specimens are shown in Figure 11.

Discussion

Any method of analysis of renal calculi must take account of the salient fact that the majority of urinary stones from adults in developed countries are composed either of calcium oxalate virtually alone, or of mixtures of calcium oxalate and phosphate. This finding has been reported by numerous groups and was previously reported for this laboratory (Westbury, 1974). Table I shows that in the present series about 55% of the stones fall into these categories. It therefore has to be shown that TG analysis coped adequately with these stones. Figure 1 shows that the 'pure' calcium oxalate stones can in fact be well analysed by TG analysis alone. However, it is also true that TG analysis alone can be successfully applied to the calcium oxalate and phosphate mixtures because of the lack of weight loss shown by the main phosphates of calcium on heating. The presence of phosphate can therefore be inferred by the reduced oxalate content, correspondingly increased ash and absence of positive indications of all other compounds. Brushite, $CaHPO_4.2H_2O$, loses its water of crystallisation at about 100°C but this mineral is a rather rare ingredient of renal stones (Herring, 1962; Lonsdale, Sutor and Wooley, 1968). In fact the correlation between oxalate found by TG analysis and standard chemical techniques, must be regarded as highly satisfactory (see Fig. 2). There was a tendency for the chemical value to be slightly higher than the TG value, probably due to the presence in the calculi of reducing substances, other than oxalate which would interefere with the permanganate titration. It is therefore concluded that calcium oxalate can be accurately measured in renal calculi by TG analysis.

Nakano (1922-23) appears to have been first to recognise that calcium oxalate occurs in renal calculi both as a monohydrate (Whewellite) and as a dihydrate (Weddelite). Jensen (1940)



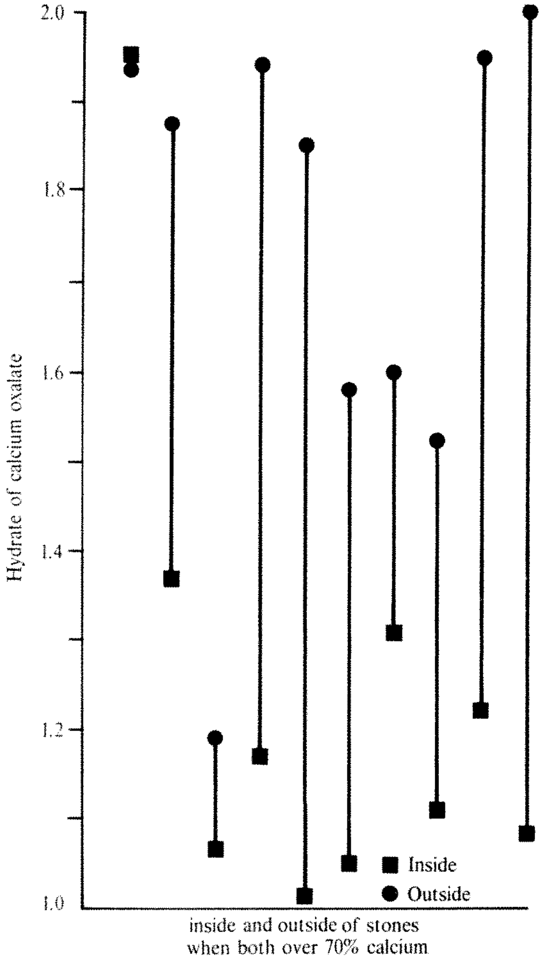


Fig. 10 (left). Degree of hydration of calcium oxalate in a series of 103 renal calculi, each of which contained more than 70% calcium oxalate. Only 23 are pure mono- or dihydrate and the rest must be mixtures of these two hydrates in varying proportions.

Fig. 11 (right). Degrees of hydration of calcium oxalate in 10 renal calculi where samples from both inside and outside contained over 70% calcium oxalate. In every case except one, the outside stone showed the higher degree of hydration.

observed that both types appeared in the same calculi and this has since been confirmed by numerous authors (Prien and Frondel, 1947; Pyrah, 1958; Strates, 1966; Elliot, 1973). There have been disagreements, however, about the significance of this observation. Jensen (1940) thought that the calcium oxalate was laid down as dihydrate and that it subsequently lost a molecule of water so undergoing conversion to the monohydrate. Prien and Frondel (1947), however, gave several reasons for believing this theory to be incorrect and thought that both monohydrate and dihydrate could be precipitated directly from urine on to the stone surface. Elliot (1973) studied 150 ureteral stones by polarised light microscopy and found mainly monohydrate in the centres and mainly dihydrate at the periphery, so confirming the preliminary report of Strates (1966). Similar findings were reported by Bellonato *et al.* (1973). Elliot thought that monohydrate was laid down as such in the nucleus and that dihydrate was precipitated later on to the existing surface of monohydrate. Hösli (1957), however, demonstrated that the dihydrate turned into the monohydrate in renal calculi *in situ* and this was confirmed by Cifuentes Delatte *et al.* (1973). This still does not completely dispose of the matter, since the same group (Bellanato *et al.*, 1973) admitted the further possibility that both monohydrate and dihydrate may be precipitated separately or together. It therefore seemed worth examining the data presented here for the state of hydration of calcium oxalate in renal stones to see if it lent support to any of the theories described.

Figure 11 shows that there is a marked tendency for the degree of hydration of calcium oxalate to fall on passing from the surface towards the nucleus of a stone. This was clearly the case for 9 of 10 renal calculi where appropriate data could be obtained, so supporting the findings of others (see above). The 10th proved to be almost pure dihydrate throughout, supporting the view of Jensen that the calcium oxalate is laid down as dihydrate and that the occurrence of monohydrate arises from loss of water in already laid down dihydrate. If this theory is correct, one might expect to find a relationship between weight of stone and the degree of hydration, with the smallest stone being richest in dihydrate.

Figure 10 shows that in the series of 103 renal calculi, each of which contained over 70% calcium oxalate, the degree of hydration varied greatly. Relatively few were pure monohydrate or pure dihydrate, most being mixtures. A whole range of mixtures was found, although perhaps the most common mixture was 10% dihydrate and 90% monohydrate (hydration 1·1). No correlation could be demonstrated between weight and degree of hydration, perhaps because small renal calculi are not necessarily newly formed. One might in fact speculate that small stones are of recent formation when they are mainly dihdyrate and old when monohydrate. Clearly, however, more work is needed to prove this point.

TG analysis of renal calculi made of magnesium ammonium phosphate presents special problems. Although the TG tracing given by magnesium ammonium phosphate is readily identified (Fig. 3), it unfortunately bears a considerable resemblance to that of Brushite (Fig. 5). Furthermore, as shown above, phosphates of calcium occur in the majority of renal stones whose main ingredient is magnesium ammonium phosphate. Therefore although the TG tracing of a given stone may have an appearance consistent with pure magnesium ammonium phosphate, it is impossible to be sure that it does not contain Brushite even in large amounts unless chemical analysis has also been performed. This consideration goes part of the way to explain the poor correlation shown in Figure 4 between magnesium content of stone and the weight loss when converted to magnesium ammonium phosphate. Thus, the presence of Brushite in a stone would mean that the total weight loss on heating would be greater than expected from consideration of magnesium content alone. Other factors, however, operate in the opposite direction. It is difficult to obtain the dry stone powder without some of the Struvite ($MgNH_4PO_4.6H_2O$) undergoing spontaneous loss of water to yield Newberyite ($MgHPO_4.3H_2O$) (Lonsdale and Sutor, 1966). Finally, total weight change must include the combustion of matrix and this can not be distinguished from loss of water and ammonia. Although these difficulties in interpreting the magnesium ammonium Phosphate/Brushite TG tracing interfere with calculations of the relative contents of these chemicals in a given stone, they do not interfere with the practical interpretation. This is because the TG tracing with the appearance due to magnesium ammonium phosphate or Brushite can be equated with infection as the cause of the stone regardless of the precise content of each ingredient and this is probably the most important fact which one is trying to establish when analysing these stones.

The results therefore confirmed that the main ingredients of renal calculi other than the phosphates of calcium, can be detected by TG analysis. They also show that the type of stone can often be identified by TG analysis alone. Table I shows that in the current series 62·8% of the stones could have been successfully analysed by the TG method alone. In a further 31·3% of the stones, TG analysis yielded useful information, although supporting data from other techniques was required in order to obtain full characterisation of the calculi. In only 6% of the stones were the TG tracings so complex as to be unhelpful and some of these (1% of the total) proved to be hoaxes or blood. The time required for an analysis was set at 35 min but the man-minutes required per analysis is very much less and 5 min is a realistic estimate. TG analysis of renal calculi has other attractions. The weight of material required is very small and it is suggested that TG analysis can be a method of first choice for all urinary calculi and that further chemical quantitative analysis would then only be required for the one-third of the samples where TG analysis failed to yield the whole answer. The method is free from radiation hazards, is quantitative and is cheaper to install than X-ray crystallography. Unfortunately, however, the cost of the equipment can still only be justified where large numbers of calculi are to be analysed.

The particular equipment used proved reliable and breakdowns were infrequent. Skill, however, is required in loading the sample and unloading the ash.

Summary

Thermogravimetric (TG) analysis has been used as a routine technique for renal tract stone analysis. The results obtained in a consecutive series of 502 renal stones are described and evaluated. The technique is easy, rapid and gives quantitative information about stone composition. Results were compared with quantitative data obtained by standard chemical methods. Correlation coefficients for oxalate and urate were 0·947 and 0·97 respectively. The comparison also showed that 63 % of the stones could have been correctly analysed by TG analysis alone; in an additional 31 %, TG analysis provided helpful information.

TG analysis permits the identification of the proportions of mono- and dihydrate of oxalate present in calcium oxalate. It is confirmed that the centres of calcium oxalate calculi are richer in dihydrate than the exterior surfaces.

We are grateful to the British Postgraduate Medical Federation for having financed the purchase of the Stanton-Redcroft thermogravimetric equipment.

References

Bellanato, J., Cifuentes Delatte, L., Hidalgo, A. and Santos, M. (1973). Application of infrared spectroscopy to the study of renal stones. In *Urinary Calculi*. Proceedings of the International Symposium on Renal Stone Research, Madrid, 1972. Basle: Karger, pp. 237-246.

Berenyi, M. and Liptay, G. (1971). The use of thermal analysis in medical science with special reference to nephroliths. *Journal of Thermal Analysis*, 3, 437-443.

Cifuentes Delatte, L., Hidalgo, A., Bellanato, J. and Santos, M. (1973). Polarization microscopy and infrared spectroscopy of new sections of calculi. In *Urinary Calculi*. Proceedings of the International Symposium on Renal Stone Research, Madrid, 1972. Basle: Karger, pp: 220-230.

Elliot, J. S. (1973). Structure and composition of urinary calculi. *Journal of Urology*, **109**, 82-83.

Herring, L. C. (1962). Observations on the analysis of 10,000 urinary calculi. *Journal of Urology*, **88**, 545-562.

Hodgkinson, A., Peacock, M. and Nicholson, M. (1969). Quantitative analysis of calcium-containing urinary calculi. *Investigative Urology*, **6**, 549-561.

Hösli, P. O. (1957). Über Genese und Aufbau von Harnsteinen; Inaug. Diss. Zurich.

Jensen, A. T. (1940). On concrements from the urinary tract. II. *Acta Chirurgica Scandinavica*, **84**, 207-225.

Lonsdale, K. and Sutor, D. J. (1966). Newberyite in ancient and modern urinary calculi: identification and space group. *Science*, **154**, 1353-1354.

Lonsdale, K., Sutor, D. J. and Wooley, S. (1968). Composition of urinary calculi by X-ray diffraction. Collected data from various localities. *British Journal of Urology*, **40**, 33-36.

Nakano, H. (1922-23). Beiträge zur Kenntnis der in den Harnsteinen enthaltenen Substanzen. *Journal of Biochemistry Tokyo*, **2**, 437-441.

Prien, E. L. and Frondel, C. (1947). Studies in urolithiasis; I. The composition of urinary calculi. *Journal of Urology*, **57**, 949-991.

Pyrah, L. N. (1958). The calcium-containing renal stone. *Proceedings of the Royal Society of Medicine*, **51**, 183-199.

Strates, B. S. (1966). Use of thermal gravimetry in the study of nephroliths. *Experientia*, **22**, 574-575.

Strates, B. S. and Georgacopoulou, C. (1969). Derivatographic thermal analysis of renal tract calculi. *Clinical Chemistry*, **15**, 307-311.

SUTOR, D. J. and SCHEIDT, S. (1968). Identification standards for human urinary calculus components, using crystallographic methods. *British Journal of Urology*, **40**, 22-28.

TSAY, Y. CH. (1961). Application of infra-red spectroscopy to analysis of urinary calculi. *Journal of Urology*, **86**, 838-854.

WESTBURY, E. J. (1974). Some observations on the quantitative analysis of over 1,000 urinary calculi. *British Journal of Urology*, **46**, 215-227.

WESTBURY, E. J. and OMENOGOR, P. (1970). A quantitative approach to the analysis of renal calculi. *Journal of Medical Laboratory Technology*, **27**, 462-474.

The Authors

G. Alan Rose, FRCP, MRCPath, Consultant Chemical Pathologist.
C. Woodfine, FIMLS, Biochemist

Correspondence to: G. Alan Rose, St Paul's Hospital, Endell Street, London WC2.

British Journal of Urology (1976), **48**, 413-417 ©

Allograft Nephrectomy

S. N. SINHA and J. E. CASTRO

Urological and Transplantation Unit, Royal Postgraduate Medical School, Hammersmith Hospital, London W12 0HS

The criteria for removal of failed renal allografts are not clearly defined. For such operations to be advised the effects should be known and the present investigation reports the indications, complications and results of allograft nephrectomies done at Hammersmith Hospital from 1967 until 1975.

Patients and Methods

A study has been made of 206 kidney transplants in 100 male patients and 71 female patients, whose ages ranged from 14 to 61 years. 157 of the transplanted kidneys came from cadaver donors and 49 from living donors. In 35 cases the patients received 2 or more allografts.

54 allograft nephrectomies were performed in 44 patients aged 15 to 54 years. 28 patients were male and 16 were female. 46 of the kidneys that were removed came from cadaver donors and 8 from living donors. Nephrectomies performed at the time of transplantation, because of hyperacute rejection or technical difficulties, were excluded from the study. The interval between transplantation and nephrectomy with the indications for removal are summarised in Table I.

Allograft nephrectomy was carried out within 6 weeks of transplantation in 22 instances. 19 of these kidneys never functioned: 8 because of histologically proven ischaemia, a further 8 because of proven acute rejection and 3 due to accelerated rejection. In 2 further cases the kidneys were removed following secondary haemorrhage and in another following incision of a wound abscess a sloughed kidney was removed.

On 17 occasions kidney allografts were removed between 6 weeks and 6 months after transplantation. 15 had irreversible acute rejection: in 1 case the graft was rejected and infected with multiple small abcesses and in another non-function was associated with recurrent pyrexia.

15 kidney allografts were removed at least 6 months after transplantation: there was histological evidence of chronic rejection in all of them. 1 patient also had persistent urinary tract infections with Salmonella and, in addition suffered an episode of Salmonella septicaemia. In another case the urine was persistently infected with resistant strains of Klebsiella. In 2 instances severe hypertension developed due to renal artery stenosis: in one, surgical correction of this failed to improve the clinical situation and in the other operation was technically impossible. 1 kidney was removed for polycythaemia with hypertension. On 5 occasions there was persistent pain over the graft which necessitated its removal and this was associated with pyrexia in 3 patients. 5 chronically rejected kidneys were moved to make space for another transplant and 4 of these patients also had ill-defined symptoms referable to the graft site.

Operative Technique

The surgical approach was always through the transplantation incision. On 8 occasions the wound was actually infected at the time of allograft nephrectomy. In all cases but 1 the procedure was performed extraperitoneally. Extracapsular removal of the graft was carried out in 48 instances while in 6 an intracapsular technique was used.

The arterial anastomosis for 29 transplantation operations was end-to-end internal iliac to donor renal artery. In a further 23 the renal artery was an anastomosed end-to-side with the external iliac and in the remaining 2 it was end-to-side with the common iliac. The venous

Table I

Indications for Allograft Nephrectomy at Intervals after Transplantation

<6 weeks after transplantation		6 weeks to 6 months after transplantation		> 6 months after transplantation	
				All had chronic rejection	
Accelerated rejection (3 C)	3	Acute rejection (14 C, 1 L)	15	Infection (2 C)	2
Primary non-function acute rejection (7 C, 1 L)	8	Infection (1 L)	1	Hypertension (2 C)	2
ischaemia (7 C, 1 L)	8	Recurrent pyrexia (1 C)	1	Polycythaemia and hypertension (1 L)	1
Miscellaneous secondary haemorrhage (2C)	2			Painful graft (2 C)	2
infection (1 L)	1			Painful graft with pyrexia (2 C, 1 L)	3
				Space for another transplant (5 C)	5
Total	22		17		15

C = cadaver, L = live.

anastomosis was always end-to-side with the external iliac vein. During removal of the transplanted kidneys the blood vessels were ligated individually in 44 instances, in 8 they were ligated "en masse" and in the remaining 2 the pedicle could not be identified.

Results

Mortality and morbidity are shown in Table II. 26 nephrectomies were performed without complication.

Mortality

There were 7 deaths after allograft nephrectomy: 5 were from severe haemorrhage and 2 were due to overwhelming infection.

Haemorrhage. 1 patient, with an infected wound at the time of nephrectomy, bled 24 hours after operation. No definite bleeding point could be found and 2 days later she died. Another had secondary haemorrhage on the 11th postoperative day. The right common iliac artery was ligated, subsequently the leg developed ischaemia and femoropopliteal thrombectomy was carried out. Cardiac arrest and death occurred suddenly on the 21st postoperative day. The third patient underwent emergency allograft nephrectomy for bleeding and suffered a second haemorrhage 24 hours later from which she died. Wound dehiscence and infection were indications for 2 other transplant nephrectomies: 1 was followed 3 weeks later by secondary haemorrhage but, despite ligation of the external iliac artery, there was further bleeding 3 weeks later which resulted in death. The external iliac artery of the other patient was tied above and below the anastomosis site during allograft nephrectomy because of bleeding from the arterial stump. 3 weeks later there was a recurrence of haemorrhage and death.

Infection. There were 2 cases where infection was the principal cause of death. In the first the allograft wound grew *Pseudomonas* sp., and 7 weeks after nephrectomy the patient died from septicaemia and cerebral abscess. In the

Table II

Mortality and Morbidity after Allograft Nephrectomy

Complication	< 6 weeks after transplantation	6 weeks to 6 months after transplantation	> 6 months after transplantation
Death	4	3	0
Wound infection	7	1	2
Secondary haemorrhage	2	–	–
Arterial damage	3	2	1
Haematoma	1	–	–
Deep venous thrombosis	1	–	–
Haemorrhage at operation	0	–	4
No complication	6	11	8
Total	24	17	15

second there was *Staph. aureus* infection and pyrexia: despite allograft nephrectomy the fever persisted and 6 weeks later the patient died following a cardiac arrest. Autopsy showed local infection at the site of the graft, valvular heart disease and pulmonary oedema.

Morbidity

The following complications occurred in the 37 patients who survived allograft nephrectomy.

Non-fatal Haemorrhage. There were 12 cases of haemorrhage in this series. 10 occurred at the time of nephrectomy. 4 of these were characterised by diffuse haemorrhage and all were carried out more than 6 months after transplantation: the technique used for removal on 3 occasions were intracapsular. They were treated conservatively. There were 6 cases when the external iliac artery was damaged at the time of nephrectomy. Repair was effected in 3 of these but in the other 3 reconstructive surgery was not possible and the artery was ligated. The external iliac vein was slightly damaged in 2 instances but was successfully repaired on both occasions. 2 patients survived secondary haemorrhage from the external iliac artery. In 1, bleeding occurred 10 days after operation and initially this was successfully repaired by direct suturing. However, a week later, despite sterile wound cultures, ligation of the external iliac artery was necessary for further haemorrhage. The patient is now well without claudication. The second patient, whose wound was infected with *Strep. faecaelis* and *Proteus* sp., bled from the external iliac artery 28 days after allograft nephrectomy. This was successfully dealt with by direct suturing.

Gross Wound Infection. Severe infection occurred in 10 cases: in 3 there was gross infection before nephrectomy and 2 more had a urinary infection at the time of operation. There were 5 cases which did not have pre-existing infection. Surgical drainage of pus was necessary in 3, 1 case was associated with partial wound dehiscence requiring secondary suture, and 1 developed a discharging sinus 1 year after allograft nephrectomy but this was closed by surgical intervention. The remaining cases were treated with local dressings and systemic antibiotics. Organisms isolated from the infected wounds were *Staph. areus* in 5 instances, *Pseudomonas* sp. in 2 and a mixed growth of *E. coli*, *Strep. faecaelis*, *Pseudomonas* and *Staph. aureus* in the remaining cases.

Wound Haematomas. Wound haematoma which required drainage occurred on 1 occasion: a litre of sterile, blood-stained fluid was evacuated and there were no further complications.

Deep Venous Thrombosis. Deep venous thrombosis complicated 1 case.

Outcome

7 deaths occurred soon after operation. 5 other patients died between 2 and 12 months after operation from causes unrelated to allograft nephrectomy. 17 patients received a second kidney transplant, 11 of whom are now alive with functioning grafts, one to 32 months following transplantation, and 6 subsequently died. 2 patients received a third kidney transplant and both are alive with functioning grafts 1 and 32 months following transplantation. 10 patients are on

haemodialysis in this hospital and awaiting a further kidney while 3 others are managed elsewhere on long-term haemodialysis.

Hypertension. 3 patients had their failed renal transplants removed because of hypertension: they had previously undergone bilateral nephrectomy of their own kidneys. 2 of the patients benefited and 1 did not. 1 of the former had associated polycythaemia: 4 weeks after allograft nephrectomy the patient became normocythaemic and his blood pressure was well controlled by methyldopa 0·5 g daily, although prior to nephrectomy drug therapy had failed to control this. The other successful case had previously undergone a vein bypass graft for stenosis of the transplant renal artery but this failed to correct the hypertension: after nephrectomy the patient remained normotensive with medication. Unsuccessful surgery to correct renal artery stenosis of the transplanted kidney had also been carried out in the patient whose hypertension did not improve following allograft nephrectomy.

Discussion

The indications for removal of failed allografts are not clearly defined. A prerequisite for such treatment is an assessment of the mortality and morbidity resulting from the operation.

In the series described 39/45 kidneys were removed within 6 months of transplantation, mainly because of primary non-function or acute rejection. Nephrectomy at this time was associated with 7 deaths; 14 operations resulted in complications whereas 17 were trouble free.

Wound infection was the most difficult problem. Apart from 2 deaths in which sepsis played a major role, after early nephrectomy 8 (20%) cases were infected. In other reported series infection ranged from 17% to 56% (Schweizer *et al.*, 1973; Moore and Hume, 1969). 50% of our cases which developed postoperative sepsis had significant infection of the graft or urinary tract before nephrectomy. Contributory causes of infection may be early haemodialysis causing haematomas, difficulty in closing the dead space and poor immunological resistance of the patient.

Schweizer performs nephrectomy as soon as the renal scan indicates insignificant blood flow to the allograft in the belief that this reduces the incidence of wound infection. For similar reasons Najarian (1974) suggests early nephrectomy as failed transplanted kidneys are frequently the source of local or systemic infection. It is not known whether allograft nephrectomy has any effect on presensitisation and subsequent graft survival.

We feel that the definite indications for early graft removal include local signs and symptoms related to the graft, graft infarction and severe uncontrollable hypertension. These symptoms are most likely to occur soon after non-function of the allograft and early nephrectomy is, therefore, encouraged in such cases. However, the operations are associated with a high incidence of mortality and morbidity because of the nature of the complications. It is probable that this could be reduced by immediate nephrectomy of all kidneys which fail within 6 months of transplantation.

The indication for removal of kidneys more than 6 months after transplantation is debatable (Shapiro *et al.*, 1975). In the present series 15 kidneys were removed 6 months or more after transplantation. All showed chronic rejection but in only 10 of these was there clear clinical evidence of the need to proceed to nephrectomy: 3 patients had pyrexia, 3 had hypertension, 2 had infection and 2 had a painful graft and all but 1 benefited from surgery. Of the remaining 5 patients whose kidneys were removed to make space for another transplant, 4 had vague symptoms referable to the graft and all of them improved following nephrectomy.

There have been no deaths when nephrectomy has been performed more than 6 months after transplantation. Haemorrhage at operation was the most critical complication and this occurred in 5 instances: in 4 it was associated with intracapsular nephrectomy. Wound infection complicated the operation on 2 occasions but 1 of these patients had a urinary infection at the time of nephrectomy. In 8 cases there were no postoperative complications.

We leave most chronically rejected kidneys *in situ* as they frequently contribute to the excretion of fluids and a similar policy is adopted by Gustafsson *et al.* (1973) who found that only 3/28 cases required removal. However, because of the complications of immunosuppression we discontinue this when the patients return to haemodialysis. In contrast Najarian maintains his patients on immunosuppressive therapy even after graft failure. It has recently been suggested that the non-functioning transplanted kidneys produce erythropoietin and that this reduces the need to transfuse patients when they are returned to haemodialysis (Shapiro *et al.*, 1975).

When allograft nephrectomy is undertaken, knowledge of the previous vascular anastomosis is important. Previous end-to-end arterial anastomoses are more easily ligated and secondary haemorrhage can be dealt with by simple ligation proximal to the anastomosis. When the kidney has been grafted using an end-to-end arterial anastomosis, nephrectomy is more difficult and secondary haemorrhage may necessitate ligation of iliac vessels.

Conclusions

Early allograft nephrectomy is associated with considerable mortality and morbidity which is frequently the result of the patients' poor general condition and pre-existing infection. Early nephrectomy as soon as graft failure is diagnosed and before sepsis or haemorrhage occur should help to minimise this.

When nephrectomy is performed 6 months or more after transplantation, pre-existing complications are rare and the morbidity after transplantation, pre-existing complications are rare and the morbidity of the operation is less. However, the indications for nephrectomy at this time are matters for debate.

Summary

The indications, complications and results of 54 allograft nephrectomies undertaken in 44 patients have been reviewed.

There were 7 deaths following 39 nephrectomies done within 6 months of transplantation and complications occurred in a further 14 instances. Many of these resulted from pre-existing infection. When nephrectomy was carried out 6 months after transplantation there were no deaths and morbidity was less.

If graft failure is diagnosed within 6 months of transplantation immediate nephrectomy is recommended to prevent future complications. When graft failure occurs later it is suggested that nephrectomy be undertaken only when definite indications for this are present.

References

Gustafsson, A., Groth, C. G., Halgrimson, C. G., Penn, I. and Starzl, T. E. (1973). The fate of failed renal homografts retained after transplantation. *Surgery, Gynecology and Obstetrics*, **137**, 40-42.

Moore, T. C. and Hume, D. M. (1969). The period and nature of hazard in clinical renal transplantation: I. The hazard to patient survival. *Annals of Surgery*, **170**, 1-11.

Najarian, J. S. (1974). Editorial comment. *Yearbook of Surgery*, 115.

Schweizer, R. T., Kountz, S. L. and Belzer, F. O. (1973). Wound complications in recipients of renal transplants. *Annals of Surgery*, **177**, 58-62.

Shapiro, D. J., Blumenkrantz, M. J., Shinaberger, J. H. and Coburn, J. W. (1975). Useful function of "non-functioning" renal homograft. *British Medical Journal*, 3, 140.

The Authors

S. N. Sinha, MS, MB, BS, Registrar and Commonwealth Medical Fellow.
J. E. Castro, MS, FRCS, PhD, Consultant Urologist.

Requests for reprints to: J. E. Castro.

British Journal of Urology (1976), **48**, 418 ©

Short Case Report

Appendiceal Granuloma causing Bilateral Hydronephrosis and Macroscopic Haematuria

Case Report

A 17-year-old man noted haematuria 2 weeks prior to admission. For 3 years he had had episodes of lumbago at 2 or 3-monthly intervals. Rectal examination revealed a smooth, elastic firm, fixed tumour the size of a hen's egg, at the prostatic base. Cystoscopic findings seemed to indicate secondary bladder cancer, *e.g.* retrovesical tumour. Intravenous pyelograms showed bilateral hydronephrosis. Seminal vesiculography appeared to be normal. The barium enema showed narrowing of the upper portion of the rectum by the tumour mass (Fig.). Laboratory data were within normal limits except ESR and CRP. Repeated transrectal and transvesical biopsies from the area of the tumour were performed. The histology of the specimen showed no malignancy. At laparotomy the appendix was grossly enlarged. An adhesion was found between the appendix, bladder and sigmoid colon. Appendicectomy was carried out. Histologically the appendix showed chronic inflammatory changes. There was no evidence of malignancy.

Comment

Haematuria or hydronephrosis followed by appendicitis is uncommon. Hyman and Capos (1959) reported 1 such case and Cook in 1969 could only find 6 cases of appendiceal abscess causing urinary retention between the age of 1 and 14 years, treated at the Hospital for Sick Children during a 10-year period. The diagnosis is usually established on the operating table (Tanaka *et al.*, 1974).

We would like to thank Prof. F. Matsubara of the Department of Pathology for his advice on this patient, and also Prof. K. Kuroda for permission to publish the case.

[1]K. Shimada, [1]T. Katsumi and [2]H. Fujita
[1] *Department of Urology and* [2] *Department of Surgery, Kanazawa University Hospital, Kanazawa-city, Japan*

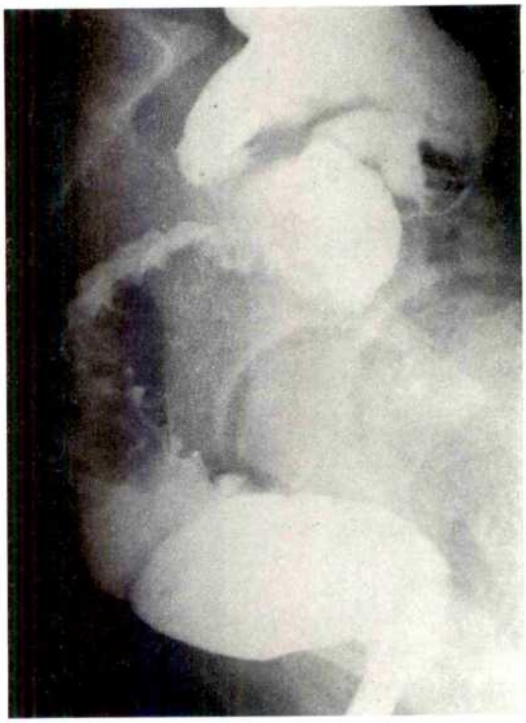


Fig.

References

Hyman, S. and Capos, N. J. (1959). Appendiceal-vesical fistula. Uncommon complication of acute perforative appendicitis with report of three cases. *Journal of the American Medical Association*, **170**, 2177-2181.

Cook, G. T. (1969). Appendiceal abscess causing urinary obstruction. *Journal of Urology*, **101**, 212-215.

Tanaka, K., Inoue, T., Nagata, M., Hirata, A. and Nakata, K. (1974). A case of ureteral stricture due to appendiceal granuloma. *Nishinihon Journal of Urology*, **38**, 151.

British Journal of Urology (1976), **48**, 419–425 ©

Embolism in a Single Functioning Kidney: Report of Two Cases

C. SELLI, D. TURINI and G. BERNI

Institute of Urology, University of Florence and Santa Maria Nuova Hospital, Florence, Italy

Embolism in a single functioning kidney is a rare cause of acute renal failure due to vascular occlusion; reviewing the world literature in English we found only 11 cases. In the future its detection will probably become more frequent. Increasing reports of renal functional recovery after disobstructive surgery (Brest, Bower and Heider, 1964; Smithwick *et al.*, 1964; Baird, Yendt and Firor, 1965; Erskine and Blaisdell, 1965; Perkins *et al.*, 1967; Peterson and McDonald, 1968; Smith, Shapiro and Messner, 1968; Fergus, Jones and Thomas, 1969; Mundth, Shine and Austen, 1969; Thomas, Faulconer and Lansing, 1969; Birkenstock, Rabkin and Stables, 1972; Morton and Crawford, 1972; Quantock and Thatcher, 1972; Sheil *et al.*, 1973; Morgan *et al.*, 1974; Smith *et al.*, 1974) and after medical anticoagulant therapy (Moyer *et al.*, 1973) have changed the attitude towards acute renal artery occlusion, which is no longer considered such a catastrophic event. This is valid even in the extreme case of a solitary kidney.

Case Reports

Case 1

A 72-year-old woman was admitted to the Urologic Clinic because of anuria which had developed 3 days earlier following left flank pain. 3 years previously she had undergone right nephrectomy for a large cyst. The patient had also a rheumatic mitral valve stenosis, with chronic atrial fibrillation. On admission her BUN was 1·8 mg %, WBC 24,000 and serum potassium 5·7 mEq/l. A retrograde pyelography did not show any obstruction. The patient was treated by haemodialysis. A radioperthecnetate renal scan was later performed, demonstrating no uptake from the left kidney (Fig. 1). Finally, retrograde transfemoral aortography showed multiple translucent emboli in the left renal artery (Fig. 2). The patient was explored through a transverse transperitoneal approach. The aorta and the left renal artery were isolated and 2 longitudinal arteriotomies were performed, 1 on the left renal artery and the other on a major branch; 5 emboli were removed. After disobstruction good back bleeding was observed from the distal artery branches, which were irrigated with Ringer lactate solution, to which heparin was added, at a temperature of 4°C. The longitudinal arteriotomies were closed transversely with 5-0 synthetic sutures to widen the vessel lumen. At the end of the procedure the kidney had resumed normal colour and good pulse could be palpated in the renal artery. Urinary output began on the 3rd day after operation, reaching a peak of 500 ml the 12th day. An average of 3 dialyses a week were necessary during the postoperative course (Fig. 3). A technetium scan performed 15 days after surgery demonstrated a good uptake from the left kidney (Fig. 1). Unfortunately the patient died 22 days after surgery with symptoms of cerebral embolism. Permission for autopsy was not granted.

Case 2

A 72-year-old woman was admitted with left hemiparesis, hypotension and severe oliguria. She was known to have a rheumatic mitral valve stenosis and 1 year earlier had a femoral artery embolectomy. An aortography performed before that intervention had also shown complete left renal artery occlusion. At hospital admittance BUN was 0·54 mg %, WBC 15,000 and serum potassium 4·4 mEq/l. Anticoagulant therapy with sodium warfarine (Coumadine) was immediately begun, and a regimen of limited salt intake was started. Retrograde transfemoral aortography demonstrated an embolus inside a major branch of the right renal artery (Fig. 4). After a week the urinary output decreased to 50 ml/day, BUN raised to 1·19 mg/10 ml serum potassium to 6·5 mEq/l and serum creatinine was 6 mg/100 ml (Fig. 5). It seemed likely that more branches of the renal artery were obstructed by emboli arising from

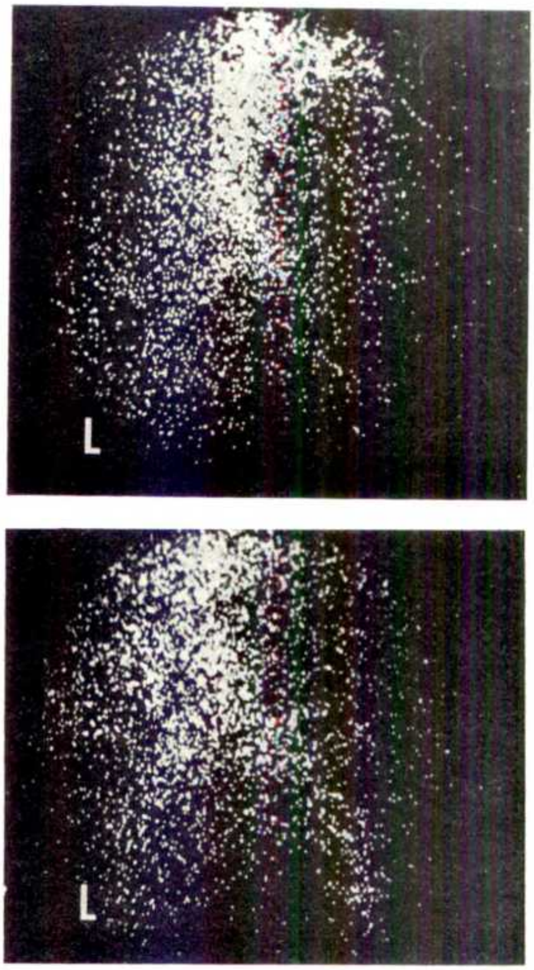


Fig. 1 Case 1; perfusion radionuclide study with technetium-99M. Posterior view. *Top:* preoperatively; poor perfusion of the left kidney. *Bottom:* 15 days after surgery; improved perfusion of the left kidney. (Previous right nephrectomy.)

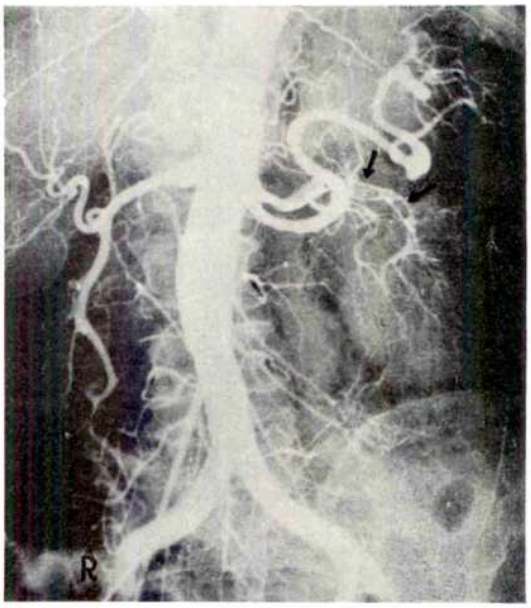


Fig. 2 Case 1; retrograde transfemoral aortography: arrows indicate translucent emboli inside the left renal artery.

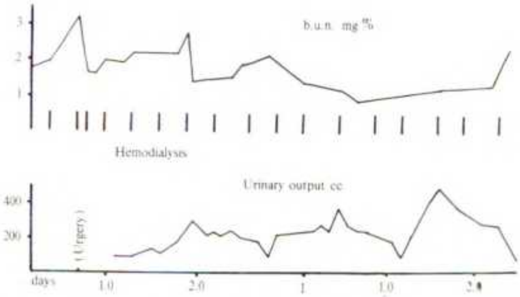
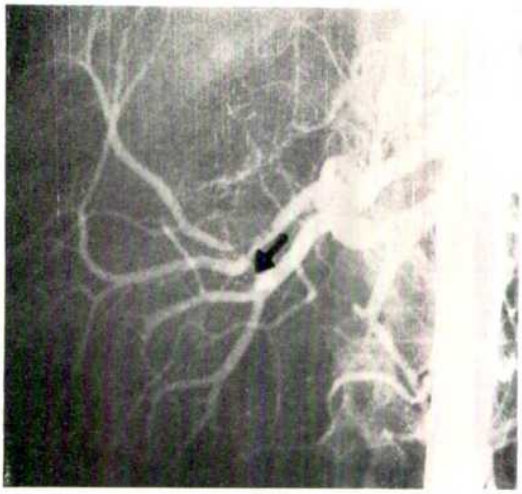


Fig. 3 Case 1; changes in BUN and urine output during the preoperative and postoperative period.

the left atrium. Exchange-ion resins were given orally with the purpose of reducing serum potassium concentration. Because of the critical general condition the patient was considered a poor risk for surgery. She was therefore immediately haemodialysed, and this treatment was repeated twice a week. Anticoagulant therapy was of course continued, maintaining the prothrombin time in therapeutic range. In order to improve the urinary output and the renal blood flow a single dose of 1,000 mg of frusemide was given intravenously. An IVP with tomography performed 3 months after her admission (Fig. 6) demonstrated a small right kidney (length 10 cm, width 4 cm) with an irregular outline, late opacification of the cavities and grouping of the calyces on the upper pole. The right kidney surface, measured on the X-ray film, was calculated to be 30 sq cm while 3 months before it had been 63 sq cm. On her discharge from hospital the urinary output was 800 cc/day, BUN 0·80, serum creatinine 3·8 mg/100 ml, serum potassium 4·7 mEq/l.

Discussion

It is not rare to find renal infarction at autopsy (Hoxie and Coggin, 1940; Schoenbaum, Goldman and Siegelman, 1971) and some authors have pointed out that there is a discrepancy between



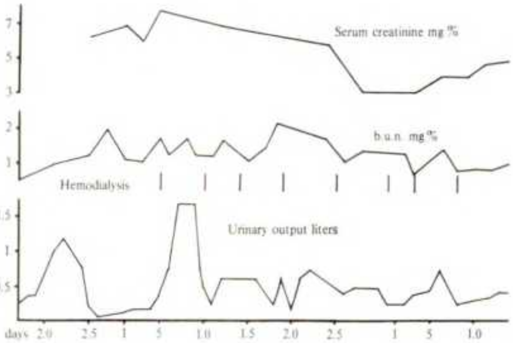
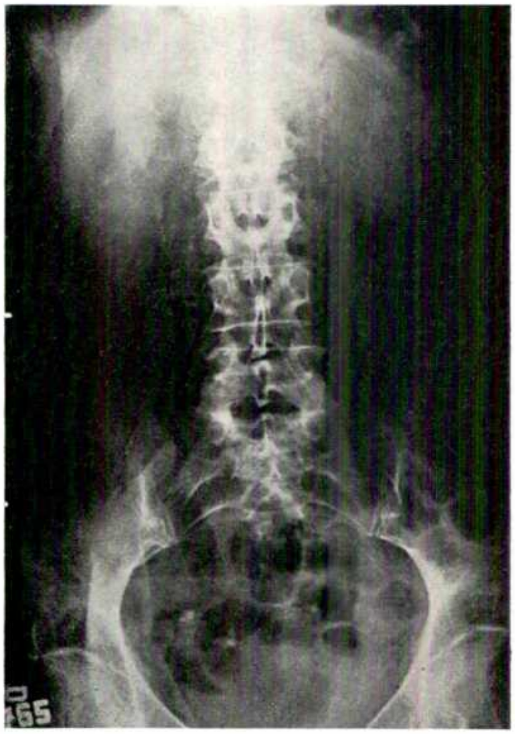


Fig. 4 (left). Case 2; retrograde transfemoral aortography: embolic occlusion of a major branch of the right renal artery.

Fig. 5 (right). Case 2; changes in serum creatinine, BUN and urine output during hospitalisation.



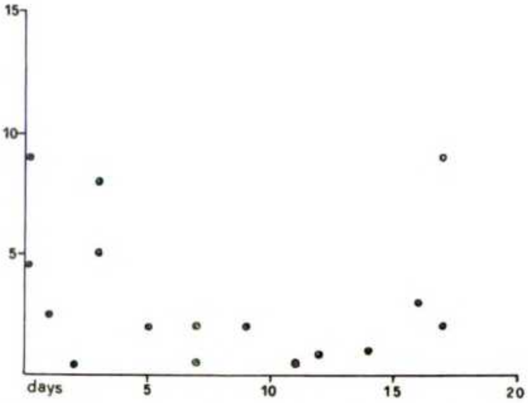


Fig. 6 (left). Case 2; IVP performed 3 months after renal artery embolisation: small kidney with irregular outlines and grouping of the calyces on the upper pole.

Fig. 7 (right). Graphic showing the absence of correlation between the duration of preoperative anuria and the length of the recovery period in 16 cases of surgically treated renal artery occlusion.

these findings and the relatively scarce number of clinically recognised cases (Sullivan *et al.*, 1972; Schramek *et al.*, 1973).

The presence of a single functioning kidney doubles the risk of damage, but makes easier the recognition of arterial obstruction, since the symptom of anuria or severe oliguria is constant. This finding, often associated with flank pain, stimulated towards a prompt angiographic investigation. Sometimes the symptoms of occlusion of other arteries are present at the same time (*e.g.* neurologic disturbances, myocardial or mesenteric infarction).

The patient's history is of paramount importance, for it often reveals that there is functional absence of a kidney and the presence of a potential source of emboli, generally heart disease with fibrillation.

Arteriography is by far the most accurate diagnostic tool in case of renal artery obstruction. Not only does it reveal the exact site of obstruction, but it has also a prognostic value, showing the development of a collateral circulation, or a certain amount of flow around the emboli.

Both factors result in a nephrographic effect, which demonstrates the presence of viable renal parenchyma. In this case a functional recovery can reasonably be expected after embolectomy. However (Sproul, 1969; Lacombe, 1971) even angiographically silent kidneys can still be viable, and surgery may be effective.

Until a few years ago it was believed, according to experimental studies, that acute renal artery occlusion caused irreversible lesions after a period of 90 min., in normothermic conditions (Kerr *et al.*, 1960).

If this were so, the problem would be of little clinical interest, since it would be very difficult to treat the patients in the short time interval. On the contrary a considerable amount of clinical reports and more recent experiments have increased our knowledge of the collateral circulation which is established even in the case of acute obstruction. Therefore acute vascular renal failure in man is an entity quite different from some experimental situations; as a matter of fact, reviewing the literature, we can observe that:

1. There is no correlation between the duration of preoperative anuria and the length of the recovery period, ranging from revascularisation to the return of the renal function (Fig. 7).
2. In most cases a correlation can be demonstrated between the development of collateral circulation and the precocity of renal functional recovery.

The collateral flow ensures to a part of the renal parenchyma a perfusion pressure of at least 15 mm/Hg. This pressure is sufficient for tissue survival, even if inadequate for the filtration (Morris, Heider and Moyer, 1955).

The collateral circulation development and extension depend mainly on the level of the obstruction and a more favourable result can be expected when the obstruction is situated near to the origin of the renal artery.

Collateral flow in man originates mainly from the lumbar arteries and, to a lesser extent, from the aorta directly, the gonadal, intercostal, adrenal and sometimes external iliac arteries (Abrams and Cornell, 1965). These collateral vessels communicate with 3 major systems; the capsular, peripelvic periureteric, through which a flow to the intrarenal arteries is established (Abrams and Cornell, 1965).

In the case of renal artery embolism, reflex vasoconstriction produces a loss of the renal function (Lacombe, 1971; Schoenbaum, Goldman and Siegelman, 1971) but after a few days the spasm ceases and an opacification of the distal branches can be angiographically demonstrated.

From our review of the 11 cases of embolism to a single functioning kidney all except 1 were treated surgically and the functional recovery was observed in 7 cases out of 10 (Table).

According to these figures we believe that surgical disobstruction is advisable whenever the general conditions allow it, though a severe cardiac disease, which is also the source of emboli, may sometimes contraindicate surgery.

Table

Cases of Embolism in a Single Functioning Kidney

Reference	Age	Sex	Side	Treatment	Time interval between symptoms onset and treatment	Outcome
Brest (1964)	73	M	R	Embolectomy	5 days	Functional recovery
Goldsmith (1968)	62	F	R	Embolectomy	12 hours	Death
	75	M	L	Embolectomy	4 days	Death
Lacombe (1971)	66	F	R	Embolectomy	5 days	Death
	66	M	R	Embolectomy	9 days	Functional recovery
Kaiser (1951)	66	F	R	Supportive Medical	5 days	Death
Peterson (1968)	57	F	R	Embolectomy	43 days	Functional recovery
Smithwick (1964)	63	F	R	Embolectomy Partial nephrectomy	2 days	Functional recovery
Schramek (1973)	55	F	L	Embolectomy	18 hours	Functional recovery
Sullivan (1972)	70	F	L	Embolectomy	9 days	Functional recovery
Thomas (1969)	45	M	R	Embolectomy	2 days	Functional recovery

In the case of embolism in a solitary kidney embolectomy is recommended when the main trunk of the renal artery is occluded; in this case all the kidney is in danger, and obviously every effort must be made to save it.

Modern dialysis techniques can help in equilibrating the patient's condition before operating, especially when diagnosis is made after some days of anuria. Haemodialysis is of course vital in the postoperative period, supporting the patient until tubular ischaemic damage is repaired.

When angiography demonstrates the occlusion of a distal branch and the general condition is poor, medical anticoagulant therapy is advisable (Lacombe, 1971).

The efficiency of local fibrinolytic treatment ceases a few hours after vascular occlusion and is therefore of little clinical advantage.

Some diuretics (frusemide, ethacrynic acid) improve the cortical blood flow and can be useful in reducing the ischaemic damage to the renal parenchyma (Birtch *et al.*, 1967).

"Blind" anticoagulant therapy before angiography is unacceptable, since it may complicate subsequent surgical treatment.

Back bleeding after arterial disobstruction has a great prognostic value, since it proves an adequate collateral circulation. Another favourable sign is the presence of normal kidney colour after embolectomy (Lacombe, 1971; Tse and Leberman, 1972; Schramek *et al.*, 1973).

Conclusions

We agree with some authors (Moyer *et al.*, 1973) about adopting non-operative treatment initially but only as a means of improving the patient's condition, thus reducing the risks of surgery.

Even if it is demonstrated that the renal parenchyma remains viable after acute vascular occlusion, the ischaemic damage often progresses after some weeks and tends to become irreversible.

Moreover repeated embolic extensions can cause rapid deterioration in the renal haemodynamic situation, as probably occurred in the second case that we reported.

In the case of embolism in a single functioning kidney the whole renal function is very often at stake and an aggressive approach is more justified than when the presence of a normal contralateral organ prevents renal failure.

Summary

2 cases of embolism in single functioning kidneys are reported. In the first case there was an occlusion of the main trunk of the renal artery; the patient was treated by embolectomy.

In the second case the occlusion of a major arterial branch was demonstrated; because of the bad general conditions the patient was treated with medical therapy.

The authors review the literature and the indications for embolectomy in embolism in a solitary kidney.

References

Abrams, H. L. and Cornell, S. H. (1965). Patterns of collateral flow in renal ischemia. *Radiology*, **84**, 1001-1012.

Baird, R. J., Yendt, E. R. and Firor, W. B. (1965). Anuria due to acute occlusion of the artery to a solitary kidney. *New England Journal of Medicine*, **272**, 1012-1014.

Birkenstock, W. E., Rabkin, R. and Stables, D. P. (1972). Bilateral traumatic renal artery occlusion with survival after late reconstitution of arterial flow. *British Journal of Surgery*, **59**, 915-917.

Birtch, A. G., Zakheim, R. M., Jones, L. G. and Barger, A. C. (1967). Redistribution of renal blood flow produced by furosemide and ethacrynic acid. *Circulation Research*, **21**, 869-878.

Brest, A. N., Bower, R. and Heider, C. (1964). Renal functional recovery following anuria secondary to renal artery embolism. *Journal of the American Medical Association*, **187**, 540-542.

Erskine, J. M. and Blaisdell, F. W. (1965). Acute bilateral renal artery occlusion in man. *Archives of Surgery*, **90**, 247-252.

Fergus, J. N., Jones, N. F. and Thomas, M. L. (1969). Kidney function after renal arterial embolism. *British Medical Journal*, **4**, 587-590.

Goldsmith, E. I., Fuller, F. W., Labrew, C. T. and Marshall, V. F. (1968). Embolectomy of the renal artery. *Journal of Urology*, **99**, 366-370.

Hoxie, H. J. and Coggin, C. B. (1940). Renal infarction: statistical study of 205 cases and detailed report of an unusual case. *Archives of Internal Medicine*, **65**, 587-594.

Kaiser, T. F. and Ross, R. R. (1951). Total infarction of the kidneys from bilateral arterial emboli. *Journal of Urology*, **66**, 500-505.

Kerr, W. K., Kyle, V. N., Keresteci, A. G. and Smythe, C. A. (1960). Renal hypothermia. *Journal of Urology*, **84**, 236-242.

Lacombe, M. (1971). The surgical treatment of renal artery embolism with anuria. *Surgery, Gynecology and Obstetrics*, **133**, 419-424.

Morgan, T., Johnston, W., Wilson, M., Clunie, G. J. and Gordon, R. (1974). Restoration of renal function by arterial surgery. *Lancet*, **1**, 653-656.

Morris, G. C., Heider, C. F. and Moyer, J. G. (1955). Protective effect of subfiltration arterial pressure in kidney. *Surgical Forum*, **6**, 623.

Morton, J. R. and Crawford, E. S. (1972). Bilateral traumatic renal artery thrombosis. *American Surgeon*, **176**, 62.

Moyer, J. O., Rao, C. N., Widrich, W. C. and Olsson, C. A. (1973). Conservative management of renal artery embolus. *Journal of Urology*, **109**, 138-143.

Mundth, E. D., Shine, K. and Austen, W. G. (1969). Correction of malignant hypertension and return of renal function following late renal arterial embolectomy. *American Journal of Medicine*, **46**, 985-988.

Perkins, R. P., Jacobsen, D. S., Feder, F. P., Lipchik, E. O. and Fine, P. H. (1967). Return of renal function after late embolectomy. *New England Journal of Medicine*, **276**, 1194-1195.

Peterson, N. E. and McDonald, D. F. (1968). Renal embolization. *Journal of Urology*, **100**, 140-145.

Quantock, O. P. and Thatcher, G. N. (1972). Reversible renal failure with renal artery occlusion. *British Medical Journal*, **2**, 27-28.

Schoenbaum, S., Goldman, M. A. and Siegelman, S. (1971). Renal arterial embolization. *Angiology*, **22**, 332-343.

Schramek, A., Hashmonai, M., Chaimovitz, C. and Better, O. S. (1973). Survival following late renal embolectomy in a patient with a single functioning kidney. *Journal of Urology*, **109**, 342-344.

Sheil, A. G. R., Stokes, G. S., Tiller, D. J., May, J., Johnson, J. R. and Stewart, J. H. (1973). Reversal of renal failure by revascularisation of kidneys with thrombosed renal arteries. *Lancet*, **2**, 865-866.

Smith, H. T., Shapiro, F. L. and Messner, R. D. (1968). Anuria secondary to renovascular disease. *Journal of the American Medical Association*, **204**, 176.

Smith, S. P., Hamburger, R. J., Donohue, J. P. and Grim, C. E. (1974). Occlusion of the artery to a solitary kidney. *Journal of the American Medical Association*, **230**, 1306-1307.

Smithwick, R. H., Newton, R. C., Crocker, D. H. and Harrison, J. H. (1964). Surgical management of renal hypertension. *American Journal of Surgery*, **107**, 104-120.

SPROUL, G. (1969). Total aortic occlusion with anuria: late embolectomy with survival. *Journal of Urology*, **102**, 383-385.

SULLIVAN, M. J., CRONIN, R., LACKNER, L. H. and EDWARDS, W. S. (1972). Embolization of a solitary kidney. *Journal of the American Medical Association*, **222**, 82-83.

THOMAS, T. V., FAULCONER, H. T. and LANSING, A. M. (1969). Management of embolic occlusion of renal arteries. *Surgery*, **65**, 576-583.

TSE, R. and LEBERMAN, P. R. (1972). Acute renal artery occlusion: etiology, diagnosis and treatment: report of a case with subsequent revascularization. *Journal of Urology*, **108**, 32-34.

The Authors

C. Selli, Assistant, Institute of Urology.
D. Turini, Assistant Professor, Institute of Urology.
G. Berni, Assistant Professor, Santa Maria Nuova Hospital.

British Journal of Urology (1976), **48**, 426 ©

Short Case Report

Filariasis Penis

Though filariasis is endemic in tropical countries, and a large section of the population is repeatedly exposed to filarial infestation, only a few of them suffer from the serious sequala of filariasis of scrotum and penis. In the majority of cases the only manifestation is that of filaraemia. Recently it has been suggested that there is a definite immune response against filaria, and the eosinophilia seen so frequently in these patients is only an expression of this reaction. However, recurrence following an adequate excision for scrotal mass is not unknown.

Case Report

The accompanying photograph is that of a 58-year-old patient who had rather an unusual recurrence in the sense that the recurrence involved the penile skin only. 17 years ago he had a left orchidectomy with complete excision of penile and scrotal skin for filariasis. The recurrence had involved mainly the skin on the dorsum of the penis. The resulting mass looked like a scrotum with the prepucial opening at the bottom. The mass was about 20 cm in diameter and the skin weighed about 4 kg after excision.

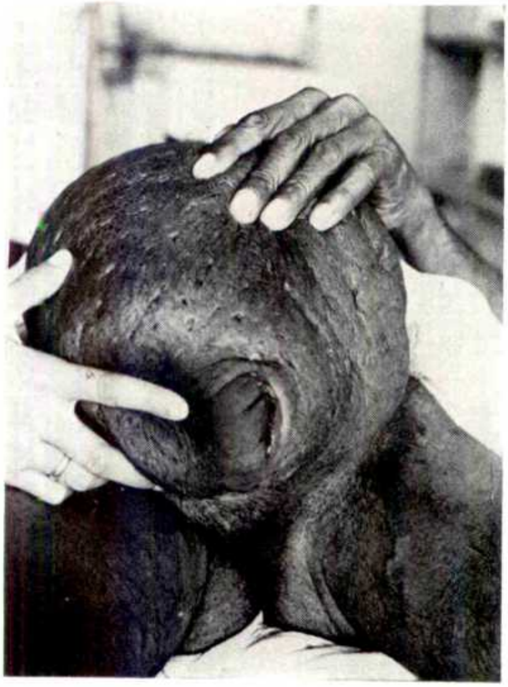


Fig. 1

Shyam Prasad
Dept. of Surgery, Rajendra Medical College Hospital, Ranchi-9, India.

British Journal of Urology (1976), **48**, 427-430 ©

Upper Urinary Tract Obstruction: Pressure/Flow Studies in Children

H. N. WHITFIELD, N. W. HARRISON, T. SHERWOOD and D. INNES WILLIAMS
Institute of Urology and St Peter's Hospitals Group, London

In children upper urinary tract dilatation may occur as the result of pelvi-ureteric or vesico-ureteric junction obstruction, but ureteric dilatation and hydronephrosis may also be found in the absence of either reflux or obstruction (Whitaker, 1975). The demonstration of obstruction as the cause of upper urinary tract dilatation may critically alter the management of a patient. Neither intravenous urography (IVU), retrograde pyelography nor renography will always allow this diagnosis to be made with certainty, but pressure/flow studies of the upper urinary tract can help to differentiate between the obstructed and the non-obstructed system.

Access to the upper urinary tract may be gained via percutaneous renal puncture, via existing nephrostomies or ureterostomies, or by direct puncture at operation (Sherwood and Stevenson, 1972; Whitaker, 1973). The pressure differential between the upper tract and the bladder at different rates of perfusion and at different bladder volumes can then be studied.

Patients and Methods

Our technique of antegrade renal puncture has already been described (Sherwood, Doyle and Williams, 1974) (Fig. 1). During the past 21 months we have investigated 24 children whose ages ranged from 4 months to 17 years with an average age of 7 years 7 months. The fact that there were 21 boys and 3 girls in the series is a reflection of the diagnoses that we were investigating (Table). Thus, 8 of the boys had upper tract dilatation following surgery for posterior urethral valves. There were 3 cases with suspected pelvi-ureteric junction obstruction, 3 patients with neuropathic bladders, 3 patients with suspected primary megaureters, 2 patients with the prune belly syndrome, 2 patients with suspected bladder neck obstruction, 2 patients with upper tract dilatation following ureteric re-implantation and 1 patient with mid-ureteric narrowing following retroperitoneal sepsis.

In the 24 children, we have studied 34 kidneys: in 1 child we studied both kidneys twice, in another child we studied 1 kidney twice and the opposite kidney 3 times; all these children had nephrostomies *in situ*. 2 children had bilateral punctures performed and in 2 children the puncture was performed on a solitary kidney.

17 of the studies were performed by renal puncture, 10 through existing nephrostomies, 5 through existing ureterostomies and 2 via direct ureteric puncture at operation. In 27 studies we were investigating the vesico-ureteric junction, in 3 the pelvi-ureteric junction, in 1 the pelvi-ureteric and vesico-ureteric junctions, in 1 case both uretero-ileal anastomoses and in 1 case the mid-ureter.

Results

Obstruction was held to be present when a pressure differential between the bladder and the upper urinary tract of more than 20 cm water developed at a perfusion rate of 10 ml/min (Sherwood

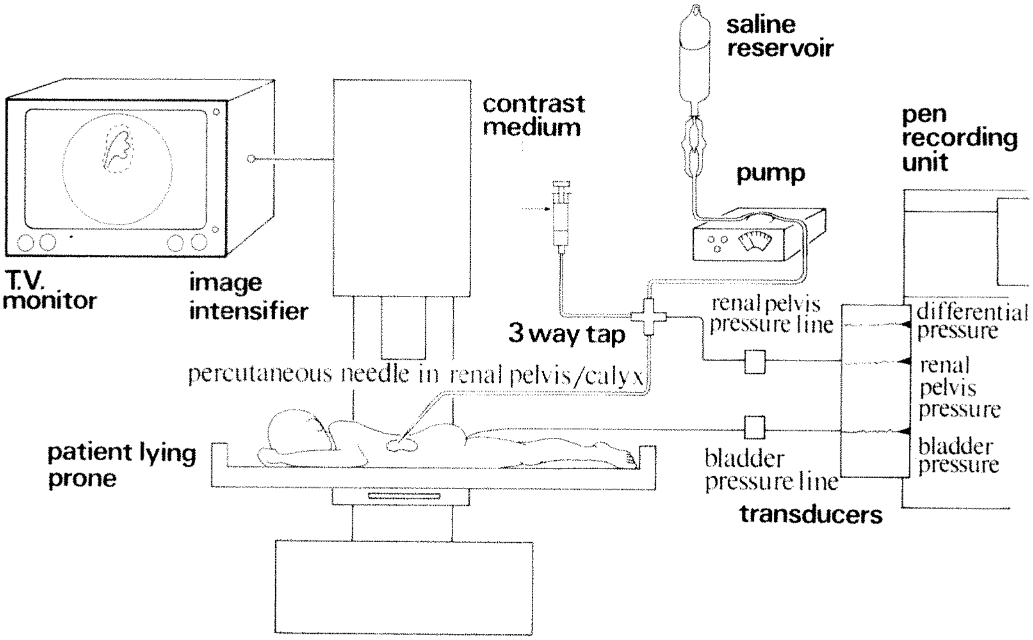


Fig. 1

Table

Diagnosis of Patients Investigated

Posterior urethral valves	8
Suspected pelvi-ureteric junction obstruction	3
Neuropathic bladder	3
Suspected primary megaureter	3
Prune Belly Syndrome	2
Suspected bladder neck obstruction	2
Dilatation after ureteric re-implantation	2
Ureteric narrowing after retroperitoneal sepsis	1

et al., 1974) or when a progressive pressure rise developed in the upper tract greater than 20 cm water.

In 21 cases no obstruction was found. In 8 cases there was evidence of obstruction, in 3 cases there was an equivocal result, and in 1 case renal puncture failed.

Discussion

Although technical difficulties were encountered, they have not been insuperable. The placing of the needle nephrostomy within a calyx is critical; unless there is free backflow, the tip of the cannula may be against the side wall of the calyx, and this can give rise to a pressure artefact. Renal puncture failed in a patient of 16 years of age with a very poorly functioning right kidney and some suggestion of vesico-ureteric obstruction on the left. Antegrade pressure studies were successful on the left and showed no evidence of obstruction; puncture attempts were unsuccessful on the right, and in view of the poor function on that side, the risks of repeated attempts did not appear balanced by the amount of useful information to be gained.

In enormously dilated systems it is sometimes quite difficult to be sure that the system has been filled, and on occasions we have had the impression that perfusion has just resulted in increased ureteric dilatation even though there has been no accompanying pressure rise. Whether or not obstruction exists in these cases is very difficult to say.

The influence of intra-vesical pressure and bladder volume on ureteric dynamics has been discussed (Zimskind, Davis and Decaestecker, 1969). The importance of performing pressure/flow studies with the bladder both empty and full has been reinforced by our experience.

Case History

A boy of 2½ years old was admitted in uraemia and found to have a solitary kidney. A nephrostomy was performed as an emergency procedure, and following this upper tract pressure studies were performed to investigate the uretero-vesical junction. Because the child had a tight phimosis it was not possible to pass a urethral catheter and the study was performed with an unknown quantity in the bladder. No evidence of obstruction was found, and on the basis of this result, the nephrostomy was removed. Following this the blood urea rose, the nephrostomy had to be replaced and a urethral catheter left *in situ*. Pressure studies were repeated and evidence of obstruction was found when the bladder was full. The vesico-ureteric junction was re-explored and a kink removed. Pressure studies following this showed no evidence of obstruction with the bladder empty or full.

There were 3 patients in whom the results were equivocal. 2 of these were in cases in whom we were able to demonstrate a pressure rise, but this rise did not reach the 20 cm water level. The third case was a patient with an occult neuropathic bladder in whom the intra-pelvic and intra-vesical pressures were grossly raised, although no differential pressure rise was demonstrated.

There was a further case in whom no obstruction was demonstrated, but in whom there seemed to be good evidence of renal functional impairment in the presence of increasing upper tract dilatation:

A girl presented in 1970 at the age of 7, with recurrent urinary tract infections. IVU at that time was normal. Because of persisting symptoms a micturating cystogram was performed in 1972 which showed left vesico-ureteric reflux to the level of the pelvic brim. Because of persistent symptoms, a Leadbetter-Politano type re-implantation was performed in December 1972 and the follow-up IVU 6 months later showed a minor degree of upper tract dilatation, but this had increased by November 1974. The ureter was re-explored and re-implanted by the advancement technique in December 1974. A follow-up IVU in July 1975 showed marked reduction in the upper tract dilatation, but because of persistent symptoms a further IVU was performed in December 1975 which showed further increase in the upper tract dilatation. In spite of the absence of demonstrable obstruction during pressure studies, it was decided to proceed with a transureteroureterostomy.

All the antegrade studies in children have been performed under general anaesthesia so that we cannot be certain what effect the drugs that have been used have on ureteric motility. There is still a lack of evidence in man about how much or how little excessive pressure is needed to cause renal deterioration. We do not know for instance whether intermittent high pressure episodes do the damage or whether renal functional impairment can occur after prolonged exposure to a continuous but low intra-pelvic pressure.

2 patients developed a Gram-negative septicaemia following the investigation; in 1 case the organism isolated on blood culture was *Proteus mirabilis* and in the other *Serratia marsescens*. These patients highlight one of the potential risks of performing antegrade pressure studies. The source of the Proteus organism was thought to be endogenous, while the Serratia organism that was isolated was most probably introduced from the perfusion apparatus. Difficulties in sterilising all components of the pump have been encountered, but more stringent aseptic precautions are now taken.

There was heavy haematuria for 24 hours in 3 cases, in 1 of whom the renal vein was known to have been punctured, but in no case was blood transfusion or exploration required.

The follow-up on the cases is short, varying from 1 month to 21 months with a mean of 6 months. It is only by long-term follow-up that the results of antegrade pressure studies can be correlated with renal function, but any such follow-up will be complicated by the difficulties of recognising static and progressive lesions of both the upper tract and of the pelvi-ureteric and vesico-ureteric junction.

Nevertheless, pressure/flow studies provide the most accurate method of diagnosing upper urinary tract obstruction at the present time. Gamma camera studies of intra-renal dynamics may provide a more precise method of diagnosis in the future. When standard radiographic, renographic and physiological investigations fail to make the diagnosis of upper urinary tract obstruction reliably, antegrade pressure studies are a valuable stand-by.

Summary

34 upper urinary tract pressure/flow studies were carried out in 24 children.

Obstruction was reliably diagnosed in 8 studies, and excluded in 21.

This technique may provide information of clinical value in the patient with upper urinary tract dilatation.

References

Sherwood, T. and Stevenson, J. J. (1972). Antegrade pyelography: a further look at an old technique. *British Journal of Radiology*, **45**, 812-820.

Sherwood, T., Doyle, P. T. and Williams, D. I. (1974). Antegrade pyelography in adults and children. *Proceedings of the Royal Society of Medicine*, **67**, 1210-1215.

Whitaker, R. H. (1973). Methods of assessing obstruction in dilated ureters. *British Journal of Urology*, **45**, 15-22.

Whitaker, R. H. (1975). Some observations and theories on the wide ureter and hydronephrosis. *British Journal of Urology*, **47**, 377-385.

Zimskind, P. D., Davis, D. M. and Decaestecker, J. E. (1969). Effects of bladder filling on ureteral dynamics. *Journal of Urology*, **102**, 693-696.

The Authors

H. N. Whitfield, MA, FRCS, Research Fellow, Institute of Urology.
N. W. Harrison, MD, FRCS, Senior Registrar, St Peter's Hospitals Group.
T. Sherwood, MRCP, FRCR, Consultant Radiologist, St Peter's Hospital Group.
D. Innes Williams, MD, MChir, FRCS, Consultant Urologist.

Requests for reprints to: H. N. Whitfield, MA, FRCS, Senior Registrar, St Bartholomew's Hospital, London, EC1.

British Journal of Urology (1976), **48**, 431–435 ©

Preliminary Communication

Diagnosis of Gross Vesico-ureteric Reflux using Ultrasonography

R. N. TREMEWAN, R. R. BAILEY, P. J. LITTLE, T. M. J. MALING, T. M. PETERS and J. J. TAIT
Departments of Medical Physics, Radiology and Renal Medicine, Christchurch Hospital, Christchurch, New Zealand

The presence of gross vesico-ureteric reflux (VUR) in infancy and childhood is associated with a high incidence of renal damage which is frequently progressive (Bailey, 1973). The part that urinary tract infection plays in the pathogenesis of this damage is still controversial (Smellie and Normand, 1975).

Currently available techniques for demonstrating VUR involve the use of either a radiographic contrast material (Maling and Rolleston, 1974) or a radioactive agent (Blaufox *et al.*, 1971; Bailey *et al.*, in press) introduced into the bladder by a urethral catheter (Blaufox *et al.*, 1971; Maling and Rolleston, 1974) or by suprapubic injection (Bailey *et al.*, in press). These are invasive techniques which involve exposure to ionising radiation.

This study was undertaken to assess a simple non-invasive ultrasonic technique for detecting gross VUR.

Methods

VUR is classified as gross when there is the radiological appearance of pronounced dilatation of the upper urinary tract with obvious ballooning of the minor calyces on the micturating cysto-urethrogram (Rolleston, Shannon and Utley, 1970). In some patients there is intrarenal extension of the reflux (Maling and Rolleston, 1974). The collecting system of a kidney with gross VUR increases in size in order to accommodate the refluxing urine. In the technique described the measurement used in the ultrasonic detection of VUR is an increase in the "renal diameter" due to the expansion of the collecting system.

The principle of the time position (TP) or M-mode is employed to obtain dynamic renal imaging. In this technique echoes are received from each tissue interface as pulsed ultrasound is propagated through the region being examined. These echoes are recorded as bright-up spots on a storage oscilloscope screen. Their horizontal displacement in time represents their distance from the transducer. Each subsequent pulse has its recorded echoes displayed vertically above the previous ones. In this way any movement of a target is recorded and seen in real time. The kidney gives an A-scan appearance of a relatively echo free area (at an appropriate depth) representing the renal parenchyma with central echoes from the pelvicalyceal system (Barnett and Morley, 1972). Figure 1 demonstrates this appearance on the TP-mode. The position of the collecting system echoes varies somewhat depending on the orientation of the probe with respect to the kidney. The pattern is, however, sufficiently typical to verify that the transducer is suitably placed.

The examinations were performed using a Diasonograph NE 4102 with a hand-held probe. Permanent records were obtained on polaroid film.

4 adults were examined using this technique. 1 had bilateral gross VUR, another unilateral gross VUR, and the third bilateral moderate VUR. The positions of the kidneys of these 3 adults

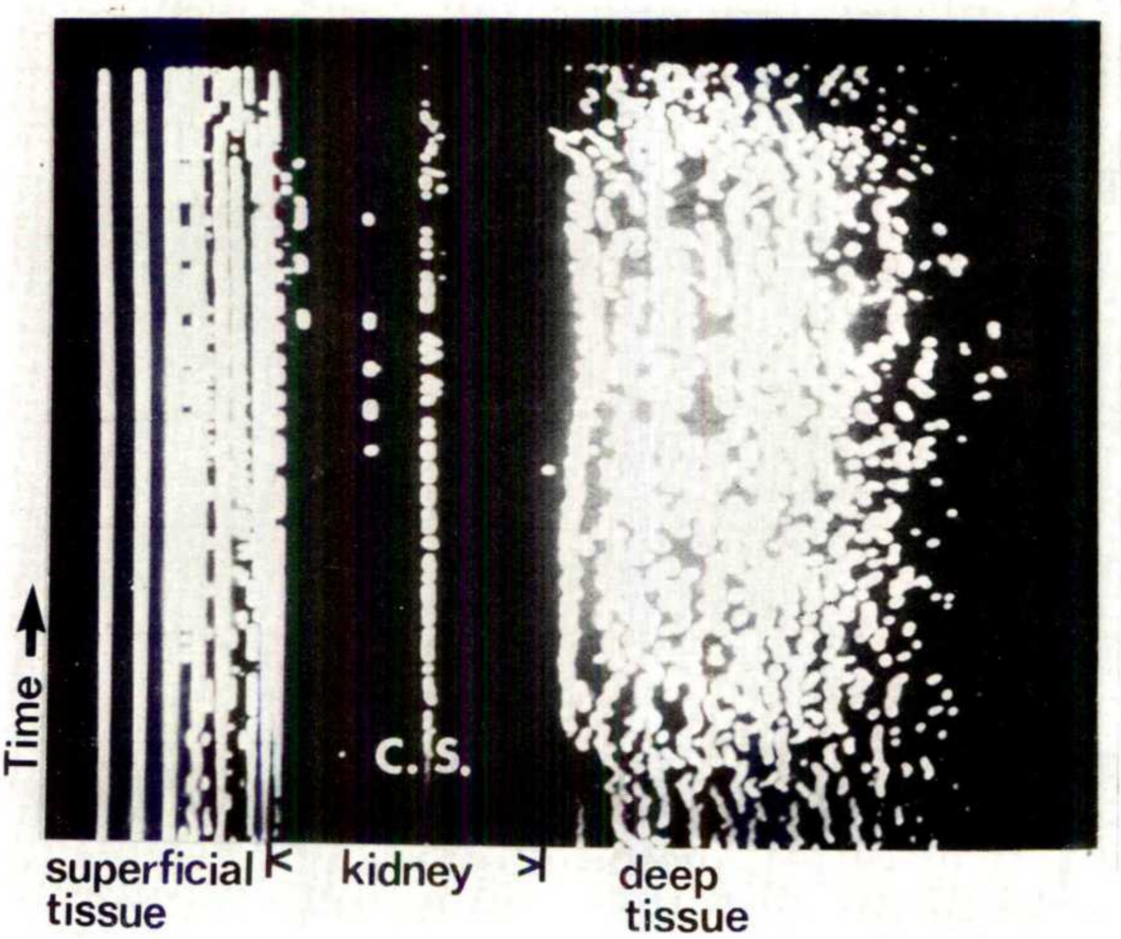


Fig. 1. The time position mode appearance of a normal kidney. CS represents the echo-complex from the collecting system of the kidney.

were initially demonstrated by ultrasonic tomography. The fourth was anephric. The presence and degree of VUR had previously been demonstrated by conventional radiological methods (Rolleston *et al.*, 1970).

The patients lay on their side for the examination. The ultrasonic transducer was positioned over the patient's kidney posteriorly. The patients had refrained from voiding urine for some time before the examination. Pressure was applied suprapubically to the patient's full bladder using the palm of the technician's hand. At the same time the borders of the kidney under observation were imaged and observed in order to detect the occurrence of any dilatation of the collecting system corresponding to the time at which the pressure was being applied.

Results

The 3 kidneys drained by ureters with gross VUR showed marked dilatation of the "renal diameter" when pressure was applied to the distended bladder. Echoes obtained from within the collecting system also showed marked changes. These appearances are demonstrated in

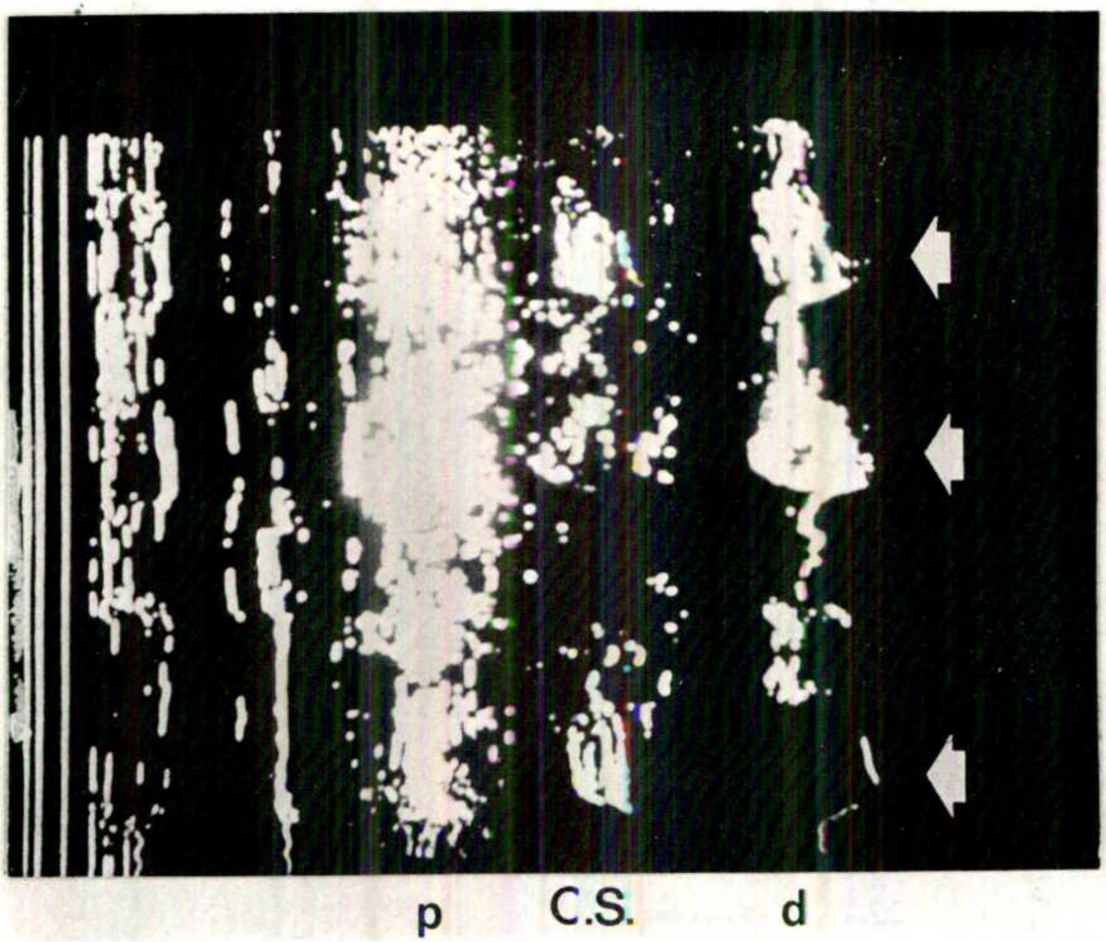


Fig. 2. Gross vesico-ureteric reflux demonstrated in a man. *p* is the border of the kidney proximal to the transducer and *d* the distal border. The arrows indicate the times at which pressure was applied to the bladder. The distal border can be seen to expand and the collecting system echoes greatly increase on each occasion.

Figures 2 and 3. The kidneys drained by ureters with moderate VUR showed some minor changes in the central echoes, but there was no detectable dilatation of the "renal diameter". The kidney drained by a ureter with no VUR showed no echo changes. In the anephric patient the renal areas examined ultrasonically showed no changes on suprapubic pressure.

Discussion

This ultrasonic technique appears to provide a safe and non-invasive method for detecting gross VUR. It is a relatively simple procedure and requires minimal co-operation from the patient. These factors make it well suited for the screening of neonates for gross VUR as well as for a general diagnostic procedure.

Provided that both sides of the kidney are well visualised and echoes from the collecting system are present, gross VUR is demonstrable with this technique. Artefactual movement due to respiration or arterial pulsation can be simply excluded firstly by the requirement that expansion of the "renal diameter" was seen to occur simultaneously with suprapubic pressure and secondly

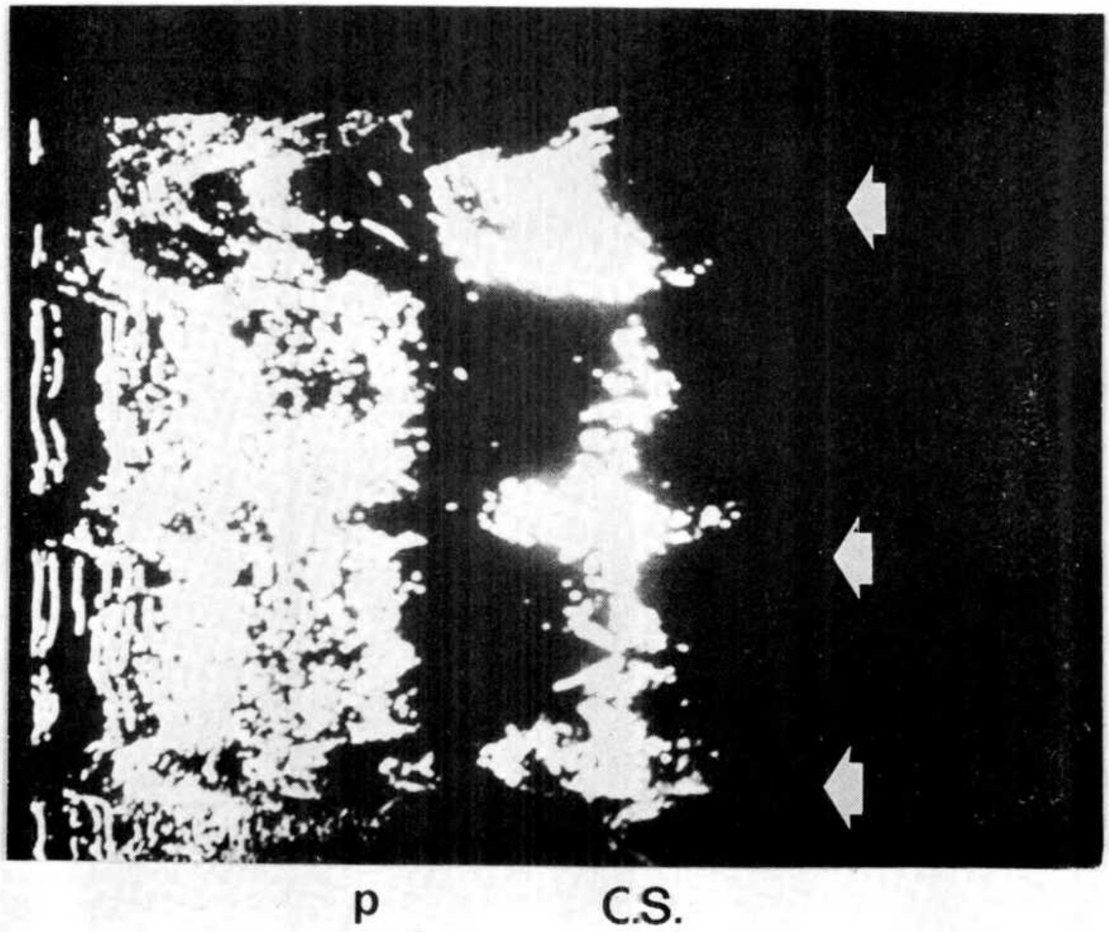


Fig. 3. Gross vesico-ureteric reflux in a man demonstrating the increase in the collecting system (CS) echoes and expansion of the renal border into the superficial tissues when pressure is applied (arrows) to the bladder. *p* is the border of the kidney proximal to the transducer. The distal border is not imaged.

that the nature of any movement seen was inflational rather than translational, *i.e.* the distal and proximal borders of the kidney moved in the opposite rather than the same direction. Patients with radiological gross VUR frequently have the reflux demonstrable while the bladder is being filled with contrast material as well as during micturition. The basic concept of this ultrasonic technique is that suprapubically applied pressure, which compares with bladder contraction, increases the dilatation of the upper urinary tract of patients with gross VUR.

Neonates and infants with gross VUR have a high incidence of renal damage when initially investigated. If this gross reflux is allowed to continue the kidneys are prone both to an arrest of normal growth and to progressive renal damage (Rolleston *et al.*, 1970, 1975). If gross VUR is diagnosed early in life it can be corrected surgically. This allows renal growth to continue and possibly prevents further renal damage occurring (McRae, Shannon and Utley, 1974).

If gross VUR could be detected very early in life reflux nephropathy might become a preventable form of chronic renal failure. The ideal would be for a screening procedure for the detection of gross VUR in the neonate (Bailey, 1973; *British Medical Journal*, 1975). The technique presented here appears to fulfil the requirements of such a procedure and warrants investigation in infants.

Summary

A simple non-invasive ultrasonic technique which identifies gross vesico-ureteric reflux (VUR) in adults is described.

It is based on the time position (TP)-mode (or M-mode) of ultrasound imaging.

This method warrants assessment as a possible screening procedure for gross VUR in newborn children.

We should like to thank Professor D. R. Aickin for the use of the Diasonograph. This work was supported by a grant from the Canterbury Medical Research Foundation. Miss Susan Small typed the manuscript.

References

BAILEY, R. R. (1973). The relationship of vesico-ureteric reflux to urinary tract infection and chronic pyelonephritis —reflux nephropathy. *Clinical Nephrology*, **1**, 132-141.

BAILEY, R. R., STAPLETON, P., TURNER, J. G. and BROWNLIE, B. E. W. Detection of vesicoureteric reflux using radionuclide micturating cystography. *Australian and New Zealand Journal of Medicine*, in press.

BARNETT, E. and MORLEY, P. (1972). Diagnostic ultrasound in renal disease. *British Medical Bulletin*, **28**, 196-199.

BLAUFOX, M. D., GRUSKIN, A., SANDLER, P., GOLDMAN, H., OGWO, J. E. and EDELMANN, C. M. (1971). Radionuclide scintigraphy for detection of vesicoureteral reflux in children. *Journal of Pediatrics*, **79**, 239-246.

British Medical Journal (1975). Vesicoureteral reflux and its familial distribution. Leading article, *British Medical Journal*, **4**, 726.

MCRAE, C. U., SHANNON, F. T. and UTLEY, W. L. F. (1974). The effect on renal growth of re-implantation of refluxing ureters. *Lancet*, **1**, 1310-1312.

MALING, T. M. J. and ROLLESTON, G. L. (1974). Intra-renal reflux in children demonstrated by micturating cystography. *Clinical Radiology*, **25**, 81-85.

ROLLESTON, G. L., SHANNON, F. T. and UTLEY, W. L. F. (1970). Relationship of infantile vesico-ureteric reflux to renal damage. *British Medical Journal*, **1**, 460-463.

ROLLESTON, G. L., SHANNON, F. T. and UTLEY, W. L. F. (1975). Follow-up of vesico-ureteric reflux in the newborn. *Kidney International*, **8**, S59-S64.

SMELLIE, J. M. and NORMAND, I. C. S. (1975). Bacteriuria, reflux, and renal scarring. *Archives of Disease in Childhood*, **50**, 581-585.

The Authors

R. N. Tremewan, BSc(Hons), ME, Medical Student.
R. R. Bailey, MD, FRACP, MRCP, Nephrologist.
P. J. Little, MB, FRCP, MRACP, Renal Physician.
T. M. J. Maling, MRACR, FRCR, Radiologist.
T. M. Peters, BSc(Hons), PhD, Physicist and Bioengineer.
J. J. Tait, MSc, MIERE, Chief Medical Physicist.

Address for reprints: Ross R. Bailey, Department of Renal Medicine, Christchurch Hospital, Christchurch 1, New Zealand.

British Journal of Urology (1976), **48**, 436 ©

Short Case Report

Appendico-vesical Fistula due to an Appendix Abscess with Associated Goblet Cell Carcinoid of the Appendix

Case Report

A 75-year-old male was admitted to the Victoria Infirmary of Glasgow in May 1974. He had a long history of prostatism with, more recently, a 3-week history of increased frequency, dysuria, nocturia and dribbling incontinence. Investigations revealed persistent coliform pyuria, a right iliac fossa mass, a separate bladder diverticulum, and an irregularity of the bladder mucosa on the right lateral wall. The prostate was assessed as Grade II benign.

Laparotomy confirmed a bladder diverticulum. Separate from this was a large fibrous mass involving the distal appendix, omentum, right vas deferens and bladder wall. The mass was removed together with appendix, bladder diverticulum and a transvesical prostatectomy carried out.

Pathology Report

The prostate and bladder tissue were entirely benign. The mass was a resolving abscess with granulation tissue involving appendix and bladder wall. The tip of the appendix was infiltrated by a mucinous adenocarcinoma showing goblet cell production and diazopositive granules. Tumour was present in the basiglandular area and spread was noted as far as serosa.

Comment

We have been unable to trace a previous report of appendico-vesical fistula associated with a primary neoplasm of appendix. Although carcinoid is the commonest appendicular neoplasm, this particular lesion is unusual, being a recently designated variant, goblet cell carcinoid of appendix (Subbuswamy *et al.*, 1974). The variant is characterised by copious production of mucin, which is predominantly acid in type; by goblet cell formation; and by argentaffin and Paneth cells. While we were unable to identify the latter, the histological features correspond with the original description.

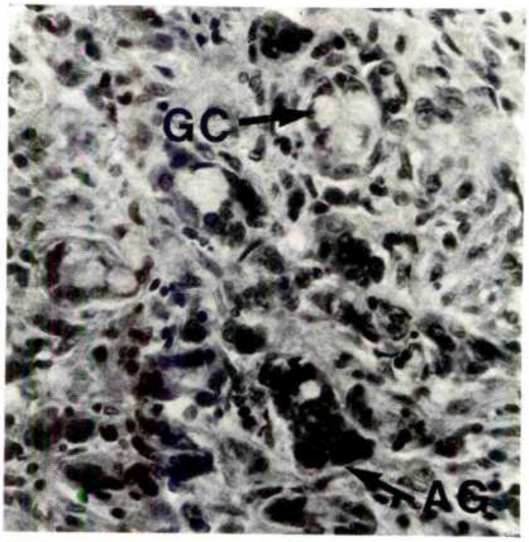


Fig. The appendicular wall is infiltrated by acini and islands with distinctive goblet cells and subnuclear argentaffin granules. GC = Acinus with goblet cells, AG = Acinus with subnuclear granules. H. & E. × 300.

We should like to thank Mr L. S. Scott for permission to publish this case and Drs J. E. Craik and B. C. Morson for helpful criticism.

M. Di Paola and W. S. Stockwell
Departments of Urology and Pathology, Victoria Infirmary, Glasgow.

Reference

Subbuswamy, S. G., Gibbs, N. M., Ross, C. F. and Morson, B. C. (1974). Goblet cell carcinoid of the appendix. *Cancer*, **34**, 338-344.

British Journal of Urology (1976), **48**, 437-441 ©

Urinary Symptoms and Total Hysterectomy

ANNE M. JEQUIER
Middlesex Hospital, Mortimer Street, London W1

Total abdominal hysterectomy may be the cause of debilitating symptoms relating to micturition. Indeed many women attend urological clinics with this problem and date the onset of their symptoms from this operation (Hanley, 1969). A large proportion of hysterectomies are performed in perimenopausal women and the incidence of micturition symptoms in women of this age-group without concomitant gynaecological disease or gynaecological surgery is very high.

It was therefore felt that a prospective study of urinary symptomatology in relation to total hysterectomy would be of interest. Such a study might help to determine the preoperative incidence of micturition symptoms in this group of women as well as the effect of hysterectomy on subjective bladder function.

Patients

Over a 1-year period, 104 women undergoing total abdominal hysterectomy were studied. The group comprised consecutive admissions for hysterectomy for a variety of gynaecological disorders. 4 women who were lost to follow-up, were excluded from the study. The youngest patient in the group was 23 years of age while the oldest was 75 years but 79% of the group were over 39 years old. All patients underwent a total abdominal hysterectomy which includes the removal of the cervix. No patient undergoing a more radical hysterectomy was studied. In 14 patients, a bilateral salpingo-oophorectomy was also performed but in all the other patients at least 1 ovary was conserved. Of those women who had a bilateral salpingo-oophorectomy, 3 were already postmenopausal.

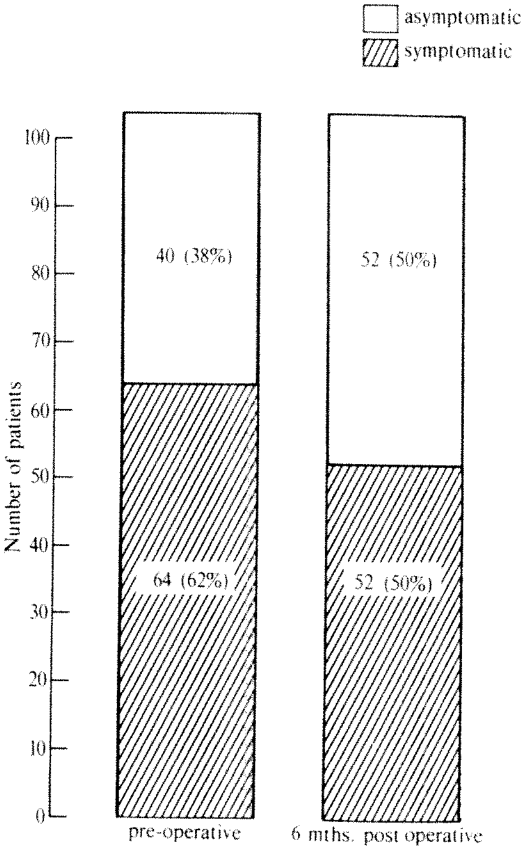
Of the 104 women studied, 45 had an enlarged uterus or ovaries constituting a pelvic mass. Such a mass was defined as an ovarian lesion of 6 inches or more in diameter or the uterus enlarged to the size of that seen in a 10-week or more gestation.

The operations were all done by members of 1 gynaecological "firm" and all were performed by surgeons of registrar, senior registrar or consultant status.

Assessment of Urinary Symptoms

The patients were interviewed preoperatively and at the gynaecological clinic 6 weeks postoperatively. 6 months after operation, the patients were asked to complete a questionnaire concerning micturition which was returned to the hospital by post.

The study was based purely on the symptomatology and no objective assessment of detrusor function or bladder neck competence was made. The presence of urinary symptoms was based on questions concerning frequency of micturition, nocturia, dysuria, urgency and urge or stress incontinence. If there was daytime frequency of micturition greater than 3 hourly or the presence of any nocturia, dysuria, urgency or incontinence, these patients were designated as being symptomatic. If dysuria was present, a mid-stream specimen of urine was obtained to exclude infection.



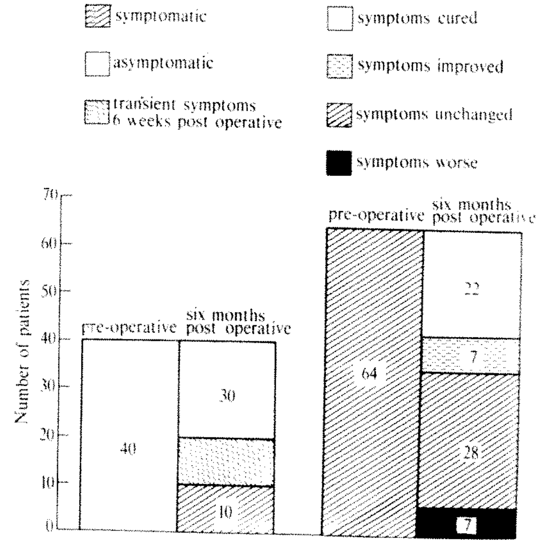


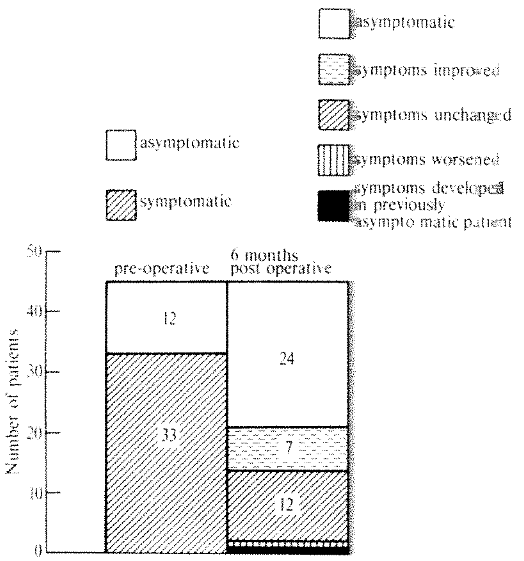
Fig. 1 (left). The incidence of urinary symptoms in 104 women before and 6 months after total abdominal hysterectomy.

Fig. 2 (right). Urinary symptoms 6 months after total hysterectomy in women who were asymptomatic and symptomatic preoperatively.

Results

Of the 104 women studied, 64 (62%) were symptomatic preoperatively and 52 (50%) were symptomatic 6 months postoperatively (Fig. 1). Frequency and nocturia were the most common symptoms. Of the 64 symptomatic patients, 39 had daytime frequency of micturition and only 2 of these women did not complain of nocturia as well. A further 3 patients complained of nocturia but gave no history of daytime frequency. A history of urgency was given by 38 of the symptomatic women and 14 complained of incontinence but only 7 of the latter group related their incontinence solely to coughing. 6 of the symptomatic women complained of dysuria but no evidence of infection was found in any 1 of them.

Of the 64 patients who were symptomatic preoperatively, 42 still had symptoms at 6 weeks after operation but the remaining 22 were symptom free at this time (Fig. 2). Of the postoperatively symptomatic women, 28 had noticed no change in symptoms, 7 were improved but not cured and 7 women had worse symptoms than were present preoperatively 6 months before. However of the 40 preoperatively asymptomatic women 10 (25%) had become symptomatic 6 months after operation and 8 had noticed transient symptoms 6 weeks after operation which had disappeared at 6 months after operation.



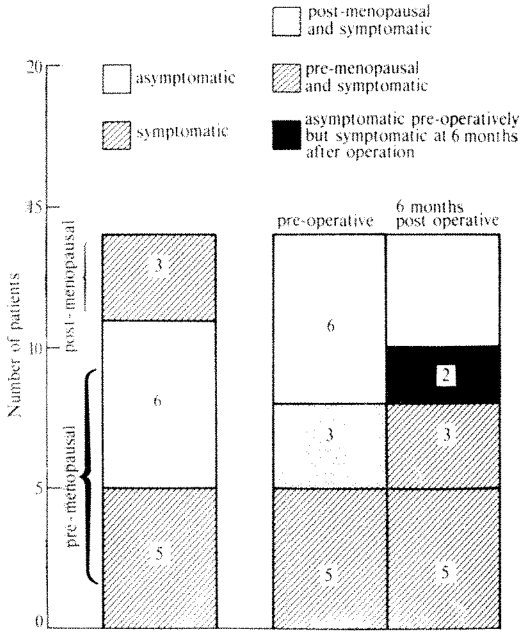


Fig. 3 (left). The effect of total hysterectomy on urinary symptoms in women with a uterine or ovarian tumour constituting a pelvic mass.

Fig. 4 (right). The effect of total hysterectomy and bilateral salpingo-oophorectomy on urinary symptoms in pre- and post-menopausal women.

Of the 45 who had a pelvic mass 33 were symptomatic preoperatively (Fig. 3). Of the symptomatic women, 12 noticed no change in their symptoms, 7 had noticed improvement but not cure, but 1 was considered worsened in this respect 6 months postoperatively. However 13 women were cured of their urinary symptoms, 6 months after operation. Only 1 patient who had been asymtomatic preoperatively had developed severe urinary symptoms at this time.

14 of 104 women underwent bilateral salpingo-oophorectomy at the time of the total hysterectomy but of these 3 were already post-menopausal at the time of operation (Fig. 4). All 3 post-menopausal women were symptomatic preoperatively and 5 of the 11 remaining pre-menopausal women were symptomatic before operation. Although none of the preoperatively symptomatic women noticed a deterioration in symptoms 6 months postoperative, none noticed any improvement and 2 of the previously asymptomatic patients now had severe urinary symptoms.

Discussion

In 1969, Hanley suggested that total hysterectomy may be the cause of debilitating and sometimes intractable urinary symptoms postoperatively. Many urologists are impressed by the large numbers of women seen in out-patient clinics who date the onset of their symptoms from such an operation. Hanley also relates this problem to total hysterectomy as it would appear that postoperative urinary symptoms were less of a problem in the days when subtotal hysterectomies were more commonly performed and the cervix was left *in situ*.

From this study, 2 features emerge. Firstly, more than half (62% of the total) had urinary symptoms preoperatively. This high incidence of micturition problems in peri-menopausal women would agree with the finding of Osbourne (unpublished) at the Middlesex Hospital who has shown that symptoms were present in 37% of women of similar age range who had no gynaecological pathology. The frequency of urinary symptoms and their variation at different times in women of this age must be considered when assessing the effects of hysterectomy on bladder function. The presence of a pelvic mass raised the incidence of preoperative symptoms as of 45 women with a pelvic mass, 33 (73%) were symptomatic before operation. Removal of the pelvic mass rendered more women asymptomatic 6 months after operation and thus the nature of the pelvic pathology must be considered when assessing the effect of hysterectomy on urinary symptomatology. Half the preoperatively symptomatic patients in this series had a pelvic mass.

Secondly from this study, a large number have their symptoms improved: of the 64 preoperatively symptomatic patients, 30 (47%) had their symptoms cured or improved 6 months postoperatively. However, 7 of the preoperatively symptomatic patients appeared to be worsened by the operation and 10 of the asymptomatic women had developed symptoms by 6 months after operation. Nevertheless, the high incidence of micturition symptoms in peri-menopausal women and the fluctuation of symptomatology that is seen in women of this age-group who have no gynaecological pathology, makes the role of total hysterectomy in the aetiology of micturitional disturbances very difficult to assess.

If total hysterectomy is responsible for micturition symptoms it is difficult to understand how such symptoms are brought about as total hysterectomy has not been shown to alter detrusor function (Brown *et al.*, 1973). Also no case of bladder neck incompetence was found on post-hysterectomy videocystography in Brown's series. In fact, it is extremely difficult to alter detrusor function surgically even when such an effect is the prime object of the procedure. Although no bacteriological studies were performed at 6 months postoperatively in this study, Smith, Roberts and Slade (1970) found a low incidence of infection in the late postoperative period and eradication of infection in affected symptomatic patients did little to alleviate their symptoms. Infection would therefore not seem to be an important cause of post-hysterectomy micturition problems.

Oestrogen deficiency has also been cited as a cause of bladder symptoms. In this series, 14 patients underwent bilateral salpingo-oophorectomy but the incidence of deterioration of urinary symptoms postoperatively was no greater in this group than in the remaining women whose ovaries were conserved. The poor response to oestrogen therapy in such women reported in other series (Smith *et al.*, 1970) would suggest that oestrogen deprivation is not an important factor in the production of micturition symptoms postoperatively.

Thus the reason why women date the onset of micturition symptoms from a total hysterectomy is difficult to ascertain. Any assessment of the incidence of micturition symptoms after hysterectomy must always be related to the high incidence of preoperative symptomatology in this group of patients. Despite the relatively large number of women totalling 17 (16%) of the 104 patients in this series who were symptomatic or whose symptoms were worsened 6 months after operation, the case against hysterectomy as a causative agent in the production of micturition symptoms remains to be proven.

Summary

A prospective study of urinary symptoms before and after total hysterectomy for a variety of gynaecological disorders has been made in 104 women.

62% were symptomatic preoperatively. Of this group 11% of the preoperatively symptomatic and 25% of the preoperatively asymptomatic either had their symptoms worsened or had symptoms appear 6 months after the operation. However, the total number of symptomatic women was reduced to 50% 6 months postoperatively.

The case against total hysterectomy in the production of urinary symptoms remains to be proven.

I am most grateful to Mr S. J. Steele, FRCS, MRCOG, Reader in Obstetrics and Gynaecology at The Middlesex Hospital, for allowing me to study his patients.

References

BROWN, A. D. G. (1973). The effect of hysterectomy on the bladder. International Continence Society. Unpublished proceedings.

HANLEY, H. G. (1969). The late urological complications of total hysterectomy. *British Journal of Urology*, **41**, 682-684.

OSBOURNE, J. (unpublished).

SMITH, P., ROBERTS, M. and SLADE, N. (1970). Urinary symptoms following hysterectomy. *British Journal of Urology*, **42**, 3-9.

The Author

Anne M. Jequier, FRCS, MRCOG, Lecturer in Obstetrics and Gynaecology (now Senior Lecturer in Obstetrics and Gynaecology, Department of Obstetrics and Gynaecology, University of Nottingham, City Hospital, Nottingham.).

British Journal of Urology (1976), **48**, 442 ©

Short Case Report

Familial Profile of Transitional Cell Carcinoma

Transitional cell carcinoma was seen in 2 families in 2 generations.

First Family

It occurred in a father and his only son (Fig. 1).

N. D. M., 83 years, male, was hospitalised in May 1969 with complaints of dysuria, frequency of urination and haematuria of 2½ months duration. IVP showed delayed excretion on right side and a filling defect on the right lateral wall of the bladder. Cystoscopy showed an extensive growth. The histopathology was transitional cell carcinoma grade III. This patient was a smoker but not exposed to any of the known carcinogenic agents.

L. D. M., 58 years, male, son of N. D. M., had an open transvesical excision of a bladder tumour in 1964. The histopathology was reported as grade II, transitional cell carcinoma. This was irradiated, but he developed haematuria requiring transurethral resection 6 months later and again in February 1972. In September 1973, histopathology showed poorly differentiated grade III transitional cell carcinoma with squamous metaplasia. His 3 children are alive and well.

Second Family

The transitional cell carcinoma was recorded in 2 brothers, whereas the other 2 brothers and 3 sisters were asymptomatic (Fig. 2).

H. L. B., 53 years, male, presented in January 1972 as a case of painless haematuria of 2 months duration. An IVP showed a poorly functioning left kidney and a large filling defect in the left half of the bladder. The patient had transurethral resection and radiotherapy. The histopathology was grade I, transitional cell carcinoma. He had a recurrence in the first 6 months requiring TUR, later on he was recurrence free.

M. L. B., 56 years, male, himself a doctor and brother of H. L. B., had painless haematuria in June 1972. IVP showed a filling defect in the right renal pelvis. Nephroureterectomy with excision of a cuff of bladder was done. The histopathology was transitional cell carcinoma. He was tumour free in the subsequent follow-up.

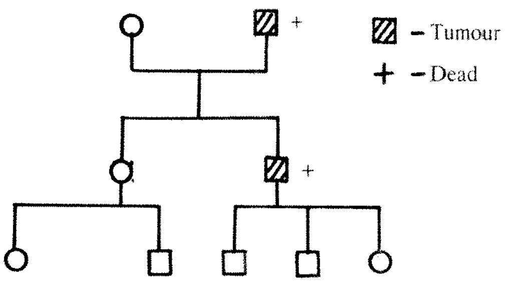


Fig. 1

Comment

Fraumeni and Thomas (1967) reported on the familial clustering of transitional cell carcinoma. McCullough *et al.* (1975) went a step further and tried to explain such an occurrence on a genetic basis. Although it might be a chance event, the mode of transmission in these 2 families appears to be consistent with autosomal dominant trait. In the first instance, the father and his son, whereas in the second family 2 brothers had this disease, implying that either the parents carried this mutation without expressing or the mutation occurred in the germinal tissue of one of the parents.

S. K. Sharma[1], B. C. Bapna[1] and S. M. Singh[2]
Departments of Urology, [1]Postgraduate Institute of Medical Education and Research, Chandigarh, [2]All India Institute of Medical Sciences, New Delhi, India

References

Fraumeni, J. F. and Thomas, L. B. (1967). Malignant bladder tumours in a man and his three sons. *Journal of the American Medical Association*, **201**, 507-509.

McCullough, D. L., Lamm, D. L., McLaughlin, A. P. and Gittes, R. F. (1975). Familial transitional cell carcinoma of bladder. *Journal of Urology*, **113**, 629-635.

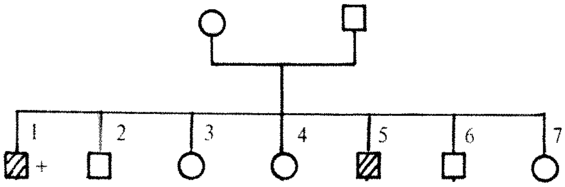


Fig. 2

British Journal of Urology (1976), **48**, 443-451 ©

The Real Bladder Electromyogram

M. D. CRAGGS and J. D. STEPHENSON

Departments of Physiology and Pharmacology, Institute of Psychiatry, London SE5

In recent years, recordings of detrusor electrical activity have become a supposedly useful diagnostic technique for investigation of various urological dysfunctions (Boyce 1952, Franksson and Petersen 1953, Jones, LaJoie and Cosgrove 1974, Doyle, Hill and Stanton 1975). For example, hypoactive and hyperactive bladders are claimed to be associated with diminished and increased low frequency (high pass filter, approx. 0·1 Hz) electromyographic activity respectively (Boyce, 1952), although Brunsting (1958) has shown that the activity is predominantly mechanical artefact. Doyle *et al.* (1975) found no correlation between very low frequency (high pass filter, approx. 0·04 Hz) electrical activity and changes in bladder pressure but nevertheless claimed an 80% correlation between the diagnosis from the detrusor EMG and that from other tests in a group of 8 patients suffering from multiple sclerosis.

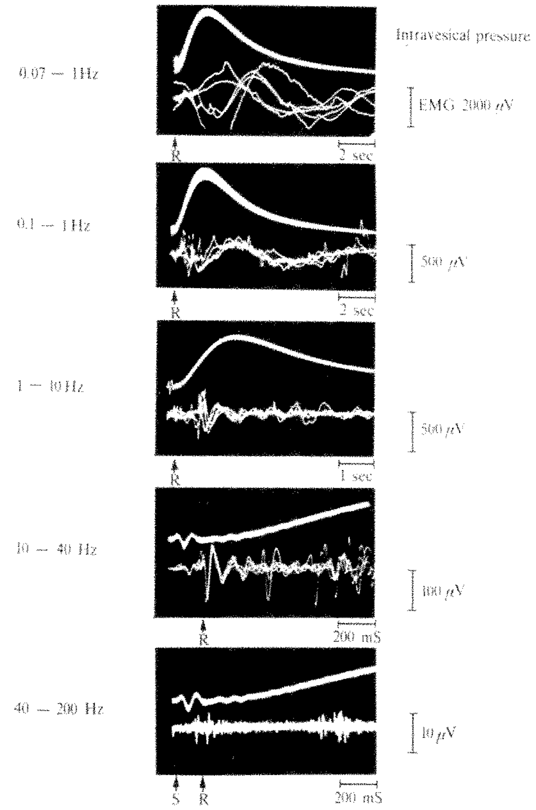
Low frequency recordings are especially prone to mechanical artefact from movements of both the bladder wall and urethra and perhaps also to electrical artefacts from adjacent smooth muscles. The present paper is an attempt to determine the contribution of real electromyogram to recordings of bladder electrical activity, and to describe methods by which this contribution may be optimised. That some real electrical activity exists in smooth muscle of the bladder was proved by Ursillo (1961) who recorded intracellular potentials from pelvic nerve-bladder strip preparations. He showed that action potentials riding on a slow depolarisation wave were often associated with small spontaneous contractions, an exact correlation with mechanical activity being seen only on nerve stimulation. Thus ventral root stimulation should provide optimal conditions for recording an evoked electromyogram in the bladder wall, assuming that the intracellular potentials are reflected extracellularly. Evoked responses have been detected in cat and baboon bladder, a preliminary account of this work being communicated to the Physiological Society (Craggs and Stephenson, 1976).

Methods

Experiments were performed on 9 cats of either sex (2·1-3 kg) and 1 male baboon (6 kg), anaesthetised with sodium pentobarbitone (36 mg/kg i.p.) and supplemented occasionally by small intravenous doses.

Pairs of insulated platinum wires (0·076 mm diameter) bared for 0·5 mm at the tips were inserted into the bladder wall from the exposed serosal surface using hypodermic needles (27 gauge). Electrodes were placed about 3 mm apart (when the bladder was about half-full) at various sites in the bladder wall but most often on its dorsal surface. With a platinum earth placed loosely in the abdomen, signals were recorded differentially on a Devices M4 recorder and AC coupled preamplifier (Type 3542) or displayed on a Tektronix storage oscilloscope (Type 549). To obtain steeper filtering than that provided by the preamplifier, additional electronic filters (VBF/3, 24 dB octave, Kemo Ltd., Beckenham) were inserted after the preamplifiers. Calibrations in each frequency band were obtained by injecting a calibration signal, whose frequency was at the mid-point of the particular band, in series with the recording electrodes.

For pelvic nerve stimulation, bilateral electrodes were placed on the appropriate sacral ventral roots, and electrical stimuli were delivered through them by a Devices Digitimer and Isolated Stimulator unit as described in the Results. Intravesical pressure was recorded from a polyethylene catheter, inserted through the bladder wall, and connected to a Statham pressure transducer and Devices M4 recorder. When required, reflex voiding was promoted by maintaining a diuresis by means of intravenous infusion of mannitol/saline (7% w/v, 1-2ml/min) and except in these experiments, the urethra was ligated.



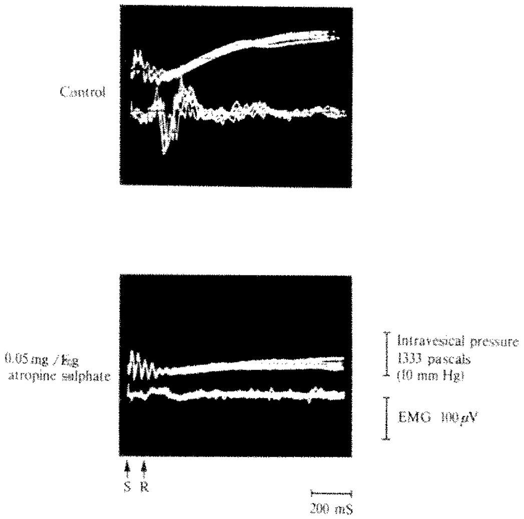


Fig. 1 (left). The effect of optimal sacral ventral root stimulation on the mechanical and electrical activity of the cat bladder in various frequency bands; 5 superimposed traces in each record. A consistent time-locked response (R) which preceded the rise in intravesical pressure, was most clearly detected in the 10–40 Hz band. The peak rise in bladder pressure was approximately 2,500 Pa. The oscillation in the intravesical pressure trace preceding the response was caused by urethral movement during stimulation. Note the different calibrations in each record. S = stimulus at the beginning of each trace.

Fig. 2 (right). The effect of atropine (0·05 mg/kg i.v.) on the optimised evoked bladder electromyogram of the baboon; 5 superimposed traces in each record. The urethral movements reflected in the intravesical pressure trace were not affected by atropine.

Results

In initial experiments, difficulty was experienced in recording electrical activity from the bladder of anaesthetised cats that could be related to intravesical pressure changes occurring during spontaneous contractions and reflex voiding. An attempt was made therefore, to see whether an evoked extracellular electromyogram could be recorded following electrical stimulation of the sacral ventral roots. A 30 ms burst of 0·5 ms pulses at a frequency of 200 pulses/s and amplitude rarely exceeding 2 V, produced a maximal sustained contraction of the bladder and a time-locked bladder electrical response to each burst of stimulation (average latency about 150 ms) which was most clearly detected within a 10-40 Hz frequency band (Fig. 1). To confirm the muscular origin of these signals, the experiment was repeated in 1 baboon. The bladder of the baboon, unlike that of the cat, is sensitive to atropine (Brindley and Craggs, 1975). As expected, atropine (0·05 mg/kg i.v.) completely abolished both the electrical response and the bladder contraction (Fig. 2).

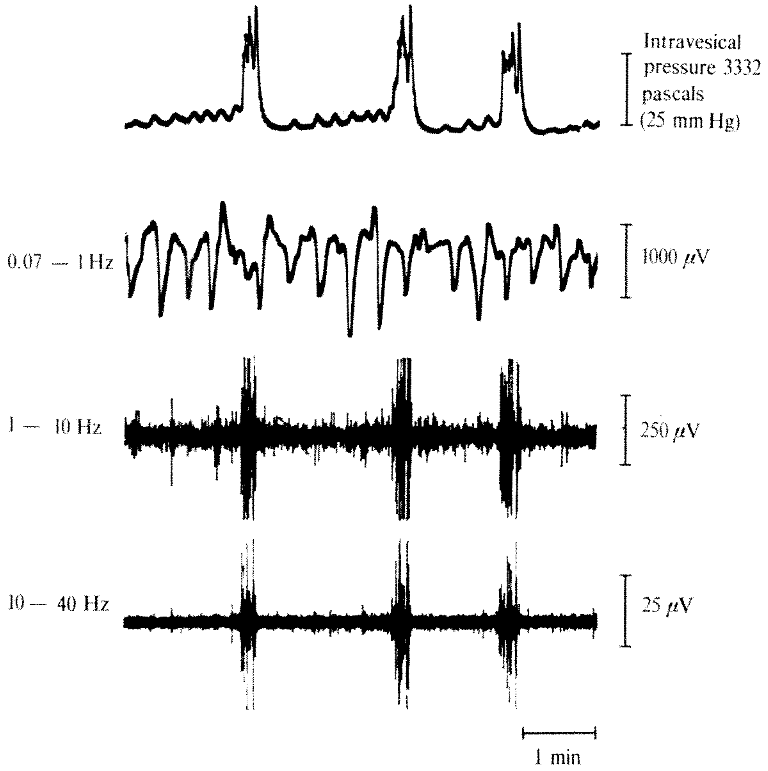


Fig. 3. Intravesical pressure changes and bladder electrical activity during reflex voiding in an anaesthetised cat. Activity in the very low frequency band (0·07–1 Hz) appeared to be random whereas activity in the other 2 bands was highly correlated with voiding.

At frequencies above 40 Hz, little could be seen of the evoked response whereas at frequencies below 10 Hz, the evoked response was swamped by activity of much greater amplitude (Fig. 1). In the 1-10 Hz band, large amplitude signals of longer latency than the evoked response but poorly time-locked to the stimulus were seen. However these only occurred during the rapid rise in intravesical pressure and never preceded the onset of bladder contraction. At frequencies between 0·07 and 1 Hz, electrical activity was completely unrelated to changes in intravesical pressure although filtering within this band (0·1-1 Hz) revealed a bladder wave which followed the evoked bladder contraction.

Figure 3 illustrates electromyographic activity recorded in 3 frequency bands during mannitol-induced reflex voiding. Only activity in the 1-10 Hz and 10-40 Hz bands consistently accompanied voiding; activity in the 0·07 to 1 Hz band was unrelated to either voiding or the small contractions preceding voiding. Activity in the 1-10 Hz band was occasionally seen in the absence of any significant activity in the 10-40 Hz band (Fig. 4), previously shown to be the optimum for recording the evoked signal. Further, this 1-10 Hz activity was not seen during the small contractions leading up to voiding (Fig. 5). During this period, only activity in the 10-40 Hz band reliably correlated with intravesical pressure. Amplitude of activity in the high frequency band remained constant during these small contractions (Fig. 5) and even during voiding itself, except when this was accompanied by obvious abdominal and pelvic contractions. In such instances, the abdominal and pelvic contractions, and their contribution to activity in the 40-200 Hz band could be abolished by succinylcholine (0·05-0·1 mg/kg i.v.).

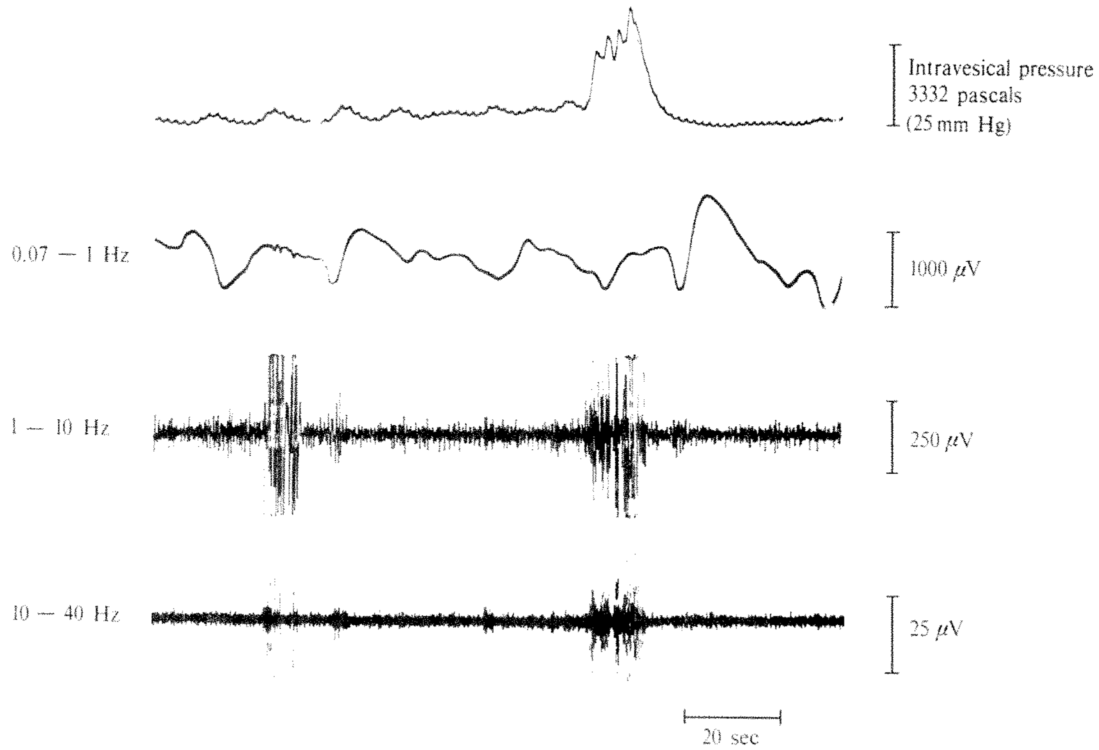


Fig. 4. Intravesical pressure changes and bladder electrical activity during reflex voiding in an anaesthetised cat. An example of dissociation between activity in the 1–10 Hz band and reflex voiding. The small increase in activity in the 10-40 Hz band in the absence of voiding can be attributed to carry-over of the large amplitude activity in the adjacent 1-10 Hz band.

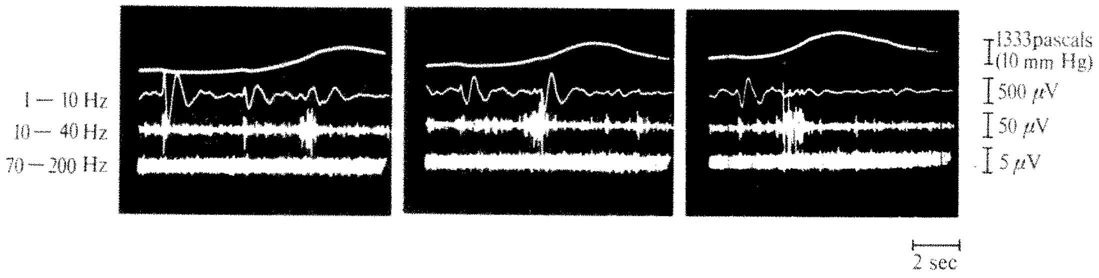


Fig. 5. Electrical activity recorded during the small contractions leading up to reflex voiding in an anaesthetised cat. Note the gradual increase in baseline intravesical pressure upon which are superimposed small spontaneous contractions and with which activity in the 10–40 Hz band is highly correlated. In this instance in the high frequency record, the high pass filter was 70 Hz rather than 40 Hz to avoid carry-over of activity from the 10-40 Hz band.

To confirm that the 10-40 Hz band was optimal for recording the evoked signal in the above experiment, the sacral roots were exposed, placed on electrodes and stimulated in the manner described. The results for a series of stimulations are shown in Fig. 6 (taken from the same pair of electrodes as in Figs. 3-5) where the evoked signal is most clearly seen against the background activity in the 10-40 Hz band, the amplitude of each response being approximately 30-40 μV.

To check the nature of electrical activity in the absence of bladder contractions, the bladder was tied, removed and placed in a bath of fresh saline at 37°C. There was a rapid decline in

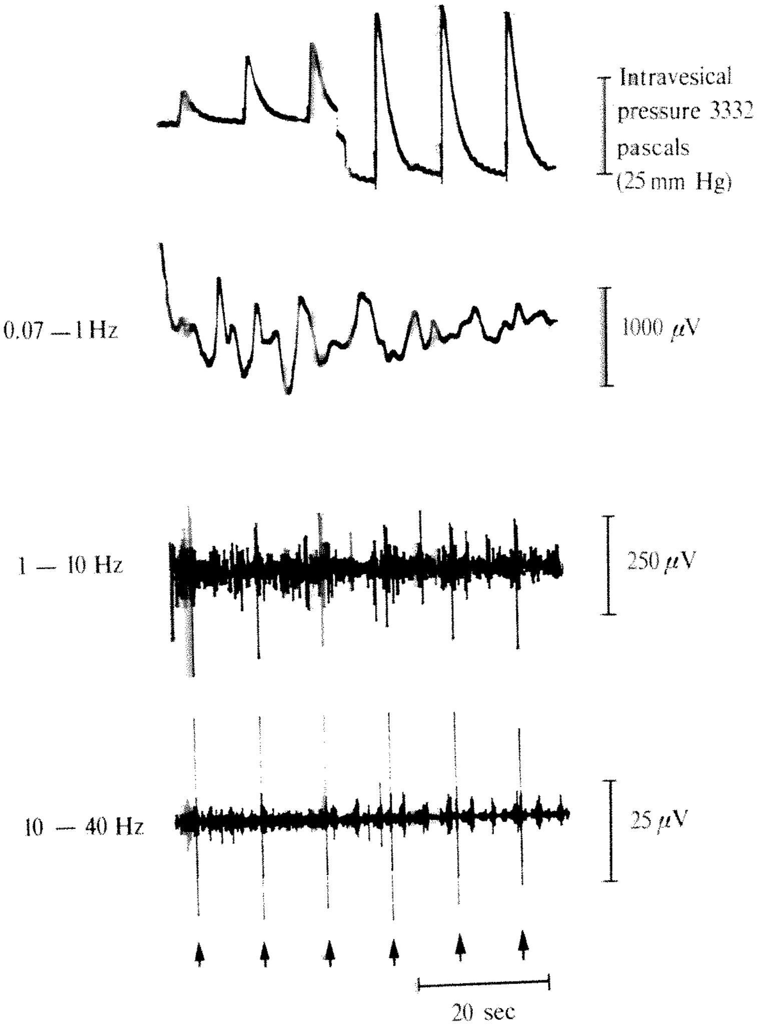


Fig. 6. Effect of optimal sacral ventral root stimulation on the intravesical pressure and bladder electrical activity in an anaesthetised cat, recorded from the same animal with the same pair of electrodes as in Figs. 3–5. Note that the signal : noise is greatest in the 10–40 Hz band. The intravesical pressure calibration scale refers to the last 3 contractions, the gain being halved for the first 3 contractions.

intravesical pressure together with attenuation of activity in the 10-40 Hz band and, to a lesser extent, in the 1-10 Hz band; activity in the 0·07-1 Hz band continued unabated (Fig. 7). 24 hours later, when the intravesical pressure record showed no evidence of contractile tone, activity in the 10-40 Hz band had almost disappeared (Fig. 7). There was some residual activity in the 1-10 Hz band but considerable activity remained in the 0·07-1 Hz band of an amplitude and frequency similar to that seen *in vivo*.

To determine whether fluid movement at the electrode tips (*e.g.* by diffusion, convection or tissue movement) could generate very low frequency waves, saline was passed from a 50 ml syringe by a syringe pump down a rigid polyethylene tube (2 mm i.d.) into which platinum electrodes were fixed. Random potentials resembling these very low frequency waves were recorded,

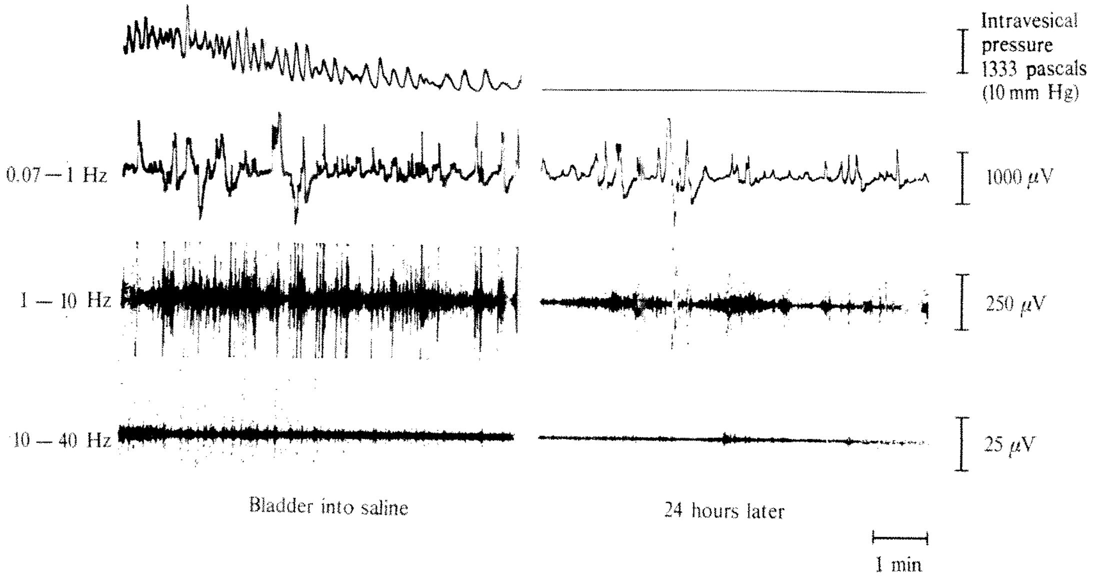


Fig. 7. Decline in mechanical activity of the excised bladder placed in a bath of saline at 37°C. Note continuation of activity in the very low frequency band after 24 hours isolation in saline.

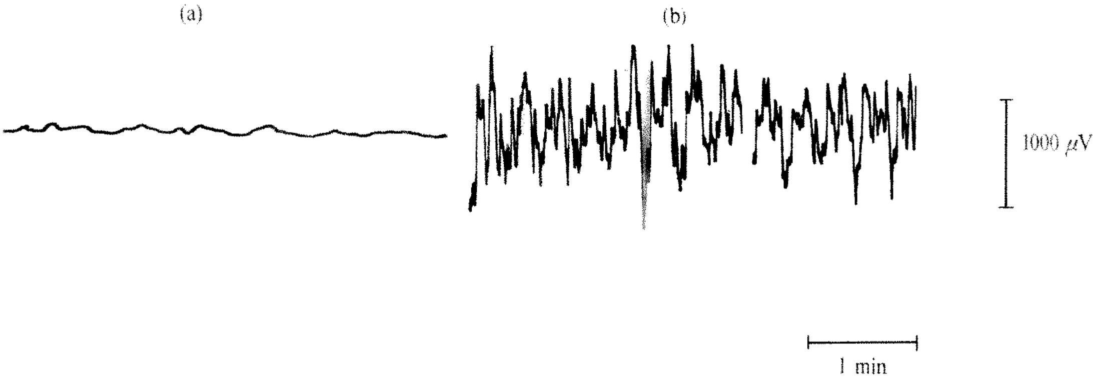


Fig. 8. Effect of saline on fixed platinum electrodes in a rigid tube (2 mm i.d.). Frequency band 0·07–1 Hz. (*a*) No flow; (*b*) flow from a syringe pump at 1 ml/min.

even at flow rates of less than 1 ml/min (Fig. 8). It appeared that these were generated by the minute fluctuations in the saline consequent upon the travel, at approximately 2·0 mm/min, of the plunger along the syringe barrel despite the electrodes and syringe being 30 cm apart, since substantially less activity was produced by a similar smooth flow from a gravity feed.

Discussion

A real electromyogram was evoked by electrical stimulation of the nerves to the bladder. This response, which preceded the onset of the bladder pressure rise by approximately 100 ms, had a duration of 150-200 ms and a latency of between 100 and 200 ms. These findings are consistent with intracellular recordings from isolated nerve-bladder strip preparations (Ursillo, 1961). This signal originated from the smooth muscle cells, rather than pre- or post-ganglionic fibres lying in

Table I

Correlation of Bladder Electrical Activity recorded in Various Frequency Bands from Anaesthetised Cats with Changes in Intravesical Pressure occurring during Reflex Voiding and during Small Spontaneous Contractions. The Predominant Source of Activity in each Frequency Band is indicated. Included also are the Frequency Bands used by Other Authors.

Frequency range	Author	High pass filter (Hz; time constant)	Approximate amplitude of recorded activity (μV)	Correlation found in present study with intravesical pressure		Predominant source of recorded activity
				During reflex voiding	During small spontaneous contractions	
Very low	Stanton Hill and Williams (1973) Doyle, Hill and Stanton (1975)	0·04; 5 s	> 500	None	None	Physico-chemical; tissue and fluid movement
	Boyce (1952)	0·1; 2 s	> 500	Some	None	Bladder movement, movement of viscera, abdominal wall, etc.
Low	Franksson and Petersen (1953) Jepson and Martin (1973) Fredericks *et al.* (1969)	2; 0·1 s	100	Good	None	Rapid movements of bladder; probably includes real signal
Medium	Craggs and Stephenson (1976)	10	50	Good	Good	Real EMG plus a contribution from the immediate lower frequency band
High	Jones, LaJoie and Cosgrove (1974)	70	20	None	None	Skeletal EMG, small amount of real signal.

the bladder wall since similar signals in baboons were abolished by atropine. The baboon bladder, unlike that of the cat, is very sensitive to atropine (Brindley and Craggs, 1975); atropine lacks effect on bladder parasympathetic ganglion (de Groat and Saum, 1976).

The evoked electromyogram was most clearly detected within a 10-40 Hz frequency band whereas published records of bladder electrical activity during spontaneous contractions have been obtained with frequency bands ranging from a few seconds to over 100 Hz. Typically very low frequency recordings have amplitudes of at least 500 μV whereas high frequency recordings are less than 50 μV. Our experiments in reflexly voiding cats show that only activity in the 1-10 Hz and 10-40 Hz bands was correlated with intravesical pressure changes. However, activity in the 1-10 Hz frequency band could be largely attributed to a mechanical artefact caused by rapid bladder contractions both during voiding and following nerve stimulation, because the activity never preceded the intravesical pressure rise but occurred during the maximum rate of pressure increase and it was not seen to accompany small spontaneous contractions. Further its amplitude was greater than that of the evoked signal. Low frequency activity in approximately the same band has previously been observed during reflex voiding (Fredericks *et al.*, 1969; Jepson and Martin, 1973).

Amplitude and frequency of activity in the 70-200 Hz frequency band have been claimed to increase during bladder filling and voiding, this relation being of diagnostic use (Jones *et al.*, 1974). However, in the present experiments, in which intravesical pressure recordings permitted a more precise study, this correlation was not found. Increases in activity were seen to coincide with contractions of adjacent skeletal muscles, particularly noticeable during sacral ventral root stimulation. These increases could be abolished by doses of succinylcholine which did not affect the bladder response.

High amplitude low frequency activity is also believed to have a use in the diagnosis of various urological dysfunctions. Boyce (1952) described a "bladder wave" associated with voidings, but this was later dismissed as mechanical artefact (Brunsting, 1958). Similar waves were seen in the present study in the upper part (0·1–1 Hz) of the very low frequency band, particularly after nerve stimulation, but in the wider frequency band (0·07–1 Hz), activity was as described by Doyle *et al.* (1975), random in nature and not related to bladder pressure changes. It could be argued that these very low frequency signals could reflect the slow membrane potentials described in intracellular recordings (Ursillo, 1961). However, this is unlikely since on nerve stimulation, which might be expected to synchronise these potentials, the very low frequency signals recorded in the 0·07-1 Hz frequency band were still unrelated to the ensuing contraction. Thus, while part of this very low frequency activity (0·1–1 Hz) is a movement artefact related to the contraction, as described by Brunsting (1958), there is a much larger amplitude random component. This very low frequency band is particularly prone to artefact, for example, from physico-chemical events occurring at the electrode tips by tissue, fluid and ion movements, etc. This proclivity is emphasised by the finding that random very low frequency activity similar to that seen in the isolated dead bladder could be generated by minute fluctuations in the flow of saline across fixed platinum electrodes in a rigid tube. The potentials seen in the isolated dead bladder may have been caused by disturbance of the bladder and electrodes by convection currents within the bath of saline. Very low frequency potentials were also recorded from electrodes fixed to the surface of a saline-filled rubber balloon placed in a bath of saline.

Conclusions

Reliable electromyograms, from which the worst of the artefact is excluded, can be recorded in the 10-40 Hz frequency band and related to changes in intravesical pressure. Nevertheless, until parallel studies of evoked responses in patients have been done, recordings of bladder electrical activity are unlikely to be useful diagnostically.

Summary

The nature of bladder electrical activity was investigated in anaesthetised cats and 1 baboon.

A time-locked muscle response to sacral ventral root stimulation was most clearly detected within a 10-40 Hz frequency band, the response preceding the rise in intravesical pressure.

During reflex voiding only activity in the 10-40 Hz band was consistently related to reflex voiding and to the small contractions leading up to voiding.

It is concluded that only a very limited part of the wide band electrical activity recorded from the bladder can be considered genuine electromyogram and that the 10-40 Hz frequency band probably excludes the worst of the artefact.

Possible sources of artefact and their relation to changes in intravesical pressure are presented in Table I.

The authors thank Professor G. S. Brindley and Mr. H. N. Whitfield (Institute of Urology) for their interest and advice in this study and the Medical Research Council for financial assistance.

References

Boyce, W. H. (1952). Bladder electromyography: a new approach to the diagnosis of urinary bladder dysfunction. *Journal of Urology*, **67**, 650-658.

Brindley, G. S. and Craggs, M. D. (1975). The effect of atropine on the urinary bladder of the baboon and of man. *Journal of Physiology*, **256**, 55P.

Brunsting, C. D. (1958). An interpretation of the urinary bladder "electromyogram" as artefact. *Journal of Urology*, **79**, 165-170.

Craggs, M. D. and Stephenson, J. D. (1976). The contribution of real electromyogram to recordings of bladder electrical activity. *Journal of Physiology*, **258**, 123-124P.

De Groat, W. C. and Saum, W. R. (1976). Synaptic transmission in parasympathetic ganglia in the urinary bladder of the cat. *Journal of Physiology*, **256**, 137-158.

Doyle, P. T., Hill, D. W. and Stanton, S. L. (1975). Electromyography of the detrusor muscle. *Journal of Urology*, **114**, 208-212.

Franksson, C. and Petersen, I. (1953). Electromyographic recording from the normal human urinary bladder, internal urethral sphincter and ureter. *Acta Physiologica Scandinavica*, **29**, Suppl. 106, 150-156.

Fredericks, C. M., Anderson, G. F., Rasmussen, E. A. and Pierce, J. M. (1969). Electrophysiology of the canine urinary bladder. *Investigative Urology*, **7**, 33-40.

Jepson, P. M. and Martin, D. C. (1973). Canine urethral electromyography. *Investigative Urology*, **11**, 149-153.

Jones, W. G., LaJoie, W. J. and Cosgrove, M. D. (1974). Electromyography in pathologic bladder. *Urology*, **4**, 186-189.

Ursillo, R. C. (1961). Electrical activity of the isolated nerve-urinary bladder strip preparation of the rabbit. *American Journal of Physiology*, **201**, 408-412.

The Authors

M. D. Craggs, PhD, Scientific Staff, MRC Neurological Prostheses Unit, Lecturer, Department of Physiology.
J. D. Stephenson, PhD, Lecturer, Department of Pharmacology.

British Journal of Urology (1976), **48**, 452 ©

Short Case Report

Long Survival after Vaginal Sarcoma Botryoides

Vaginal sarcoma botryoides is a rare, highly malignant tumour of young girls. 90% of these tumours occur under the age of 5 and usually present with vaginal bleeding, discharge and the appearance of a haemorrhagic grape-like mass protruding from the vaginal introitus. The anterior vaginal wall is more commonly involved than the posterior. The tumour infiltrates widely under the intact vaginal epithelium and later invades the vesico-vaginal or recto-vaginal septa to involve bladder or less commonly the rectum. Microscopically the oedematous myxomatous stroma contains pleomorphic cells. Larger multinucleated cells with striated fibrils in the cytoplasm can be found in most tumours and this has led to the conclusion that these tumours are embryonal rhabdomyosarcomata rather than mixed mesodermal tumours of Mullerian duct origin as considered previously (Hilgers *et al.*, 1970).

Case Report

K. M. a 2-year-old presented with a short history of vulval irritation and passing blood and a piece of "flesh" in the urine. A polypoid structure protruded from the introitus and under anaesthetic it was ascertained that the tumour which filled the vagina arose from the anterior wall near the hymen.

The bladder was normal at cystoscopy but there was induration in the urethro-vaginal septum.

Biopsy showed a variable picture of an oedematous mesenchymal structure with more cellular areas of vascular sarcomatous type containing myoblasts.

Operation 24.5.63. Total cystectomy, hysterocolpectomy, bilateral salpingectomy, right oophorectomy, partial vulvectomy and appendicectomy. The left ovary was preserved and the urine was diverted into an ileal conduit.

Histology showed extensive subepithelial vaginal invasion and penetration of the urethro-vaginal septum to involve periurethral tissues.

The child made an uneventful recovery and remains well 12 years after operation.

Comment

Because these tumours are rare, delay in diagnosis and adequate treatment is common. Many have recurred after local excision before the sinister nature of the lesion is realised. They may also be mistaken for benign vaginal or hymenal polyps, congenital cysts or embryonal carcinoma of the vagina.

Conservative surgery almost always results in local and pelvic recurrence, although an occasional cure has been reported with hysterocolpectomy alone (Ulfelder and Quan, 1947). It is relevant that half of the children dying from the disease were found to have no spread beyond the pelvis (Hilgers *et al.*, 1970). Irradiation is largely ineffective but these tumours can respond to combination chemotherapy with vincristine, actinomycin D and cyclophosphamide and they may be a useful adjunct to surgery in tumours with extravaginal spread (Hilgers, 1975).

The only hope of cure of vaginal sarcoma botryoides lies with early radical extirpation. As many tumours have already invaded perivaginal tissues, this usually requires anterior pelvic exenteration and urinary diversion. Cure rates of up to 75% for intravaginal tumours are now reported for this procedure (Hilgers, 1975).

A. E. STUART and J. MAGRI
Department of Urology, Oldchurch Hospital, Havering, London

References

HILGERS, R. D., MALKASIAN, G. D. and SOULE, E. H. (1970). Embryonal rhabdomyosarcoma (botryoid type) of the vagina. *American Journal of Obstetrics and Gynecology*, **107**, 484-502.

HILGERS, R. D. (1975). Pelvic exenteration for vaginal embryonal rhabdomyosarcoma. *Obstetrics and Gynecology*, **45**, 175-180.

ULFELDER, H. and QUAN, S. H. (1947). Sarcoma botryoides vaginae; Complete excision of tumor in infant by combined abdominal and perineal approach. *Surgical Clinics of North America*, **27**, 1240-1245.

British Journal of Urology (1976), **48**, 453-462 ©

Nephrogenic Adenoma: a form of Adenomatous Metaplasia of the Bladder. A Clinical and Electron Microscopical Study

E. A. MOLLAND, P. A. TROTT, A. M. I. PARIS and J. P. BLANDY
Departments of Morbid Anatomy and Urology, The London Hospital, and the Institute of Urology, London

Metaplasia of urothelium in response to inflammation may take many forms, *e.g.* squamous metaplasia, cystitis cystica, and cystitis glandularis. 1 form remains an enigma: this is a rare polypoid and papillary lesion, which, from the tubular and cystic structures seen on light microscopy, led Friedman and Kuhlenbeck (1950) to designate it as "nephrogenic adenoma". In commenting on the 20 cases to be reported since then, various authors have suggested that the lesion may represent neoplasm, hamartoma, or metaplasia. 2 recent cases provided an opportunity to study these lesions by electron microscopy, and so shed some light on its controversial nature. Our experience with these 2 cases has also forced us to note the extreme severity of the symptoms, and the very unsatisfactory nature of therapy for this condition. We have also studied a third case in which "nephrogenic adenoma" was associated with the development of adenocarcinoma: there has been only 1 previous report of the probable development of malignancy in this lesion (Christoffersen and Møller, 1972).

"Nephrogenic adenoma" is not as rare as reported cases might suggest (Cameron, 1975) and it is time that attention were paid to this hitherto disregarded but striking lesion which may easily be mistaken for carcinoma of the bladder on cystoscopy and may indeed represent a premalignant change. It is our hope that more detailed study of subsequent cases may in time elucidate the common aetiological factors and natural history of this condition and so provide the rationale for more satisfactory treatment.

Case Reports

Case 1. *K. A. Aged 36. Male Sudanese soldier.* At the age of 22 haematuria occurred after exertion, and bilateral renal calculi were found. Right pyelolithotomy was followed by a urinary fistula due to a residual stone in the ureter which was removed some months later. A year later left partial nephrectomy was performed and at the age of 24 a recurrent calculus was removed by pyelolithotomy from the right side: within 6 years stones had reformed in both kidneys, and both were operated on again. Since then, and for the 5 years preceding admission he had severe persistent painful frequency, with hourly micturition day and night, despite innumerable courses of antibiotics in various doses and combinations. Because of an elevated blood uric acid he was given allopurinol. Within a year his stones had recurred: there was a distended pelvicalyceal system, and renography showed impaired function. His severe frequency was exacerbated from time to time, when he had haematuria and passed clots. Prednisone, probanthine and pyridium were given without relief. Rifampicin gave a brief respite for 3 months, but the relief did not persist, and could not be repeated with a further course. His urine was repeatedly examined for tubercle bacilli and schistosoma ova with negative results, and routine cultures usually revealed *Esch. coli*, but sometimes *Strep. faecalis*.

The only other clinical feature of note was some recurrent redness and swelling of the metatarsophalangeal ankle and knee joints, attributed to gouty arthropathy, together with some conjunctivitis, but no iritis, and none of the other stigmata of Reiter's syndrome. His serological tests were repeatedly negative for syphilis: his prostatic fluid was negative for *N. gonorrhoeae*, and *Chlamydia* was never recovered.

On examination he was an intelligent Arab-Sudanese male with 3 right and 2 left renal incisions. Blood pressure 120/70 mm Hg; haemoglobin 15·6 g/100 ml; WBC 7,700/mm^3 (eosinophils 4%); sedimentation rate 17 mm/hour

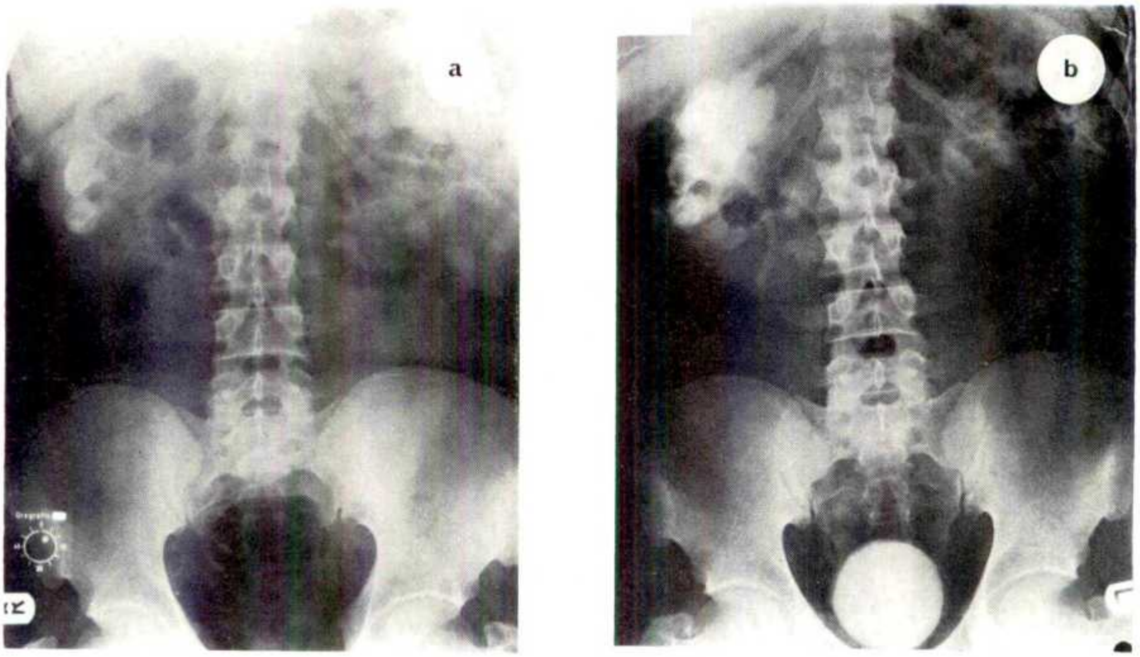


Fig. 1. Case 1. Excretion urogram showing (*a*) right renal calculus and (*b*) hydronephrosis and poor excretion on both sides.

(Westergren). Urea 38 mg/100 ml; creatinine 1·2 mg/100 ml; calcium 9·2 mg/100 ml; uric acid 9·1 mg/100 ml. No abnormality was found on rectal examination of prostate or seminal vesicles. The excretion urogram (Fig. 1) showed bilateral renal scarring and calculi. Cystoscopy revealed a uniform brick-red change in the mucosa with scattered patches of oedema resembling changes seen on other occasions in carcinoma *in situ*, which was the diagnosis made in this case. Biopsies were taken from 4 quadrants with Storz cup forceps and examined by light and electron microscopy (see below).

After further fruitless attempts to provide relief by antibiotics and antispasmodics, subtotal cystectomy was performed leaving only 0·5 cm of bladder around the internal meatus. Both ureters were divided at the mid-pelvic level and implanted by Wallace's method into the tail of an isolated ileocaecal segment (Turner-Warwick, 1976). Recovery was uneventful: by 6 weeks he had good control without frequency or pain, and after a year he wrote to say he felt really well for the first time in 12 years and had no symptoms.

Case 2. *J. M. Aged 34. English white male.* 2 years previously he underwent 2 unsuccessful attempts to remove a right ureteric calculus with Dormia's basket: after the first of these attempts he experienced severe pain and frequency. This persisted even after removal of the calculus by ureterolithotomy. He had unremitting half-hourly frequency with pain on voiding and some urethral discharge, but no haematuria. Physical examination showed him to be in good general health: blood pressure 130/80 mm Hg; Hb 15·7 g/100 ml; WBC 6,200/mm^3; urea 18 mg/100 ml. His urine failed to show *M. tuberculosis* on many attempts by staining or culture. Schistosoma ova were never found. The urine failed to yield any significant growth of other organisms on routine culture on many occasions. His excretion urogram (Fig. 2) showed a thick-walled oedematous bladder with normal upper tracts.

Endoscopy revealed widespread flat "tumour" around the neck of the bladder extending on to the lateral walls. It resembled, and was mistaken for, a carcinoma, and 4-quadrant biopsies were taken with cup forceps and examined by light and electron microscoscopy. The flat "tumour" was then thoroughly coagulated with diathermy. Despite this cystodiathermy his symptoms were unrelieved, and indeed, grew worse. In an attempt to relieve his frequency and pain Helmstein's distension method was used; but without success. 3 months later he was readmitted, now with 15 minute frequency by day and by night, and having seriously contemplated suicide.

His bladder was removed down to the internal meatus and replaced with an ileocaecocystoplasty segment, the ureters being anastomosed to the tail of the ileum by Wallace's method as in the previous case. Recovery was uneventful and 2 months later he was without symptoms, and had normal micturition, continence and sexual function.

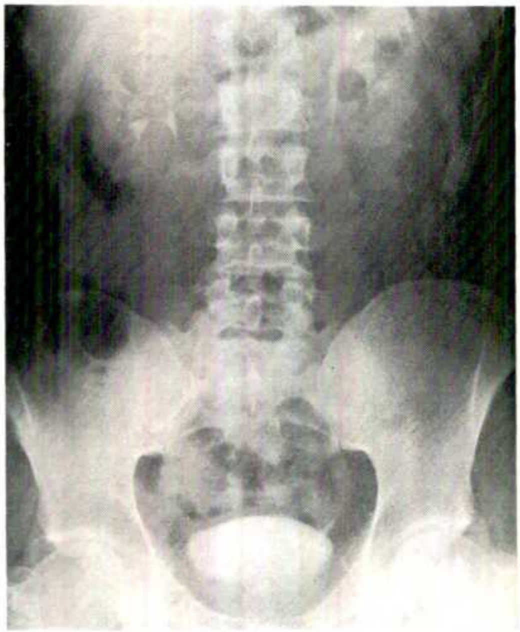


Fig. 2. Case 2. Excretion urogram showing relatively normal appearance of bladder despite intense frequency.

Case 3. *A. J. Aged 41. White male.* At the age of 22 epididymitis led to the discovery of tuberculosis with positive urine culture and a destroyed and calcified right kidney. After a course of streptomycin, PAS and isoniazid a right nephrectomy was performed, and the rest of the right ureter removed a year later. Persistent frequency from a contracted bladder was treated by anastomosis of the remaining left ureter to his sigmoid, but over the course of the next 13 years progressive hyperchloraemic acidosis necessitated diversion by an end ureterostomy, leaving the bladder behind. Since then he noticed occasional mucus passing from the urethra, but over the last year, reported that blood was sometimes mixed with this material. Accordingly cystoscopy was performed, but only oedema was seen, and the mucosa was biopsied with Storz forceps. The presence of adenomatous metaplasia in this biopsy led to regular endoscopic review at each of which a further biopsy was performed. When eventually the appearances were considered to be very possibly premalignant he was advised to undergo cystectomy. At this cystectomy an attempt was made to preserve his sexual function by sparing the prostate and seminal vesicles but unfortunately on histological examination of the specimen frank carcinoma was discovered. Accordingly a week later at a second operation a radical node dissection and *en-bloc* removal of the prostate and vesicles was carried out. His post-operative progress was uneventful.

Histology

Cases 1 and 2

In both the subtotal cystectomy specimens the mucosal surface was coarsely granular with reddish brown papillary lesions.

Tissue was fixed in formol saline, embedded in paraffin wax and stained with haematoxylin and eosin, periodic acid-Schiff (PAS) after pretreatment with diastase, Alcian blue, and by van Gieson's technique. Biopsy fragments from Case 1, and tissue from the subtotal cystectomy specimen of Case 2 were fixed in glutaraldehyde, post-fixed in osmium tetroxide, embedded in Spurr's resin (Case 1) or Araldite (Case 2) and examined in the A.E.I. electron microscope after staining with uranyl acetate and lead citrate.

In both specimens light microscopy showed papillary and polypoid areas with numerous glands lined by simple columnar epithelium extending down into the lamina propria in the first case (Figs. 3 and 4) and communicating with the surface epithelium in the second (Fig. 5). The latter was replaced by simple columnar epithelium whilst there was also some squamous metaplasia in

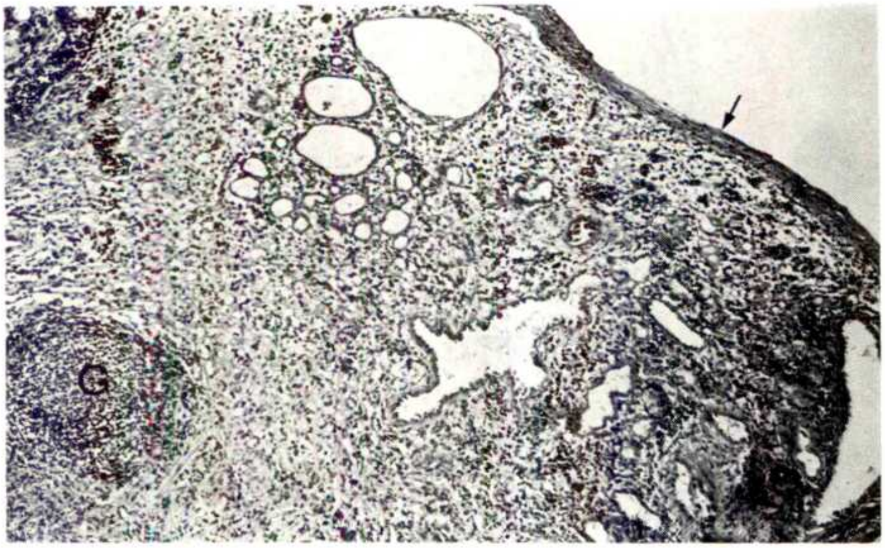


Fig. 3. Case 1. Lamina propria of bladder containing tubules some cystic with chronic inflammatory cells including lymphoid germinal centres (G). There is squamous metaplasia of the surface epithelium (arrowed) (H&E. ×40).

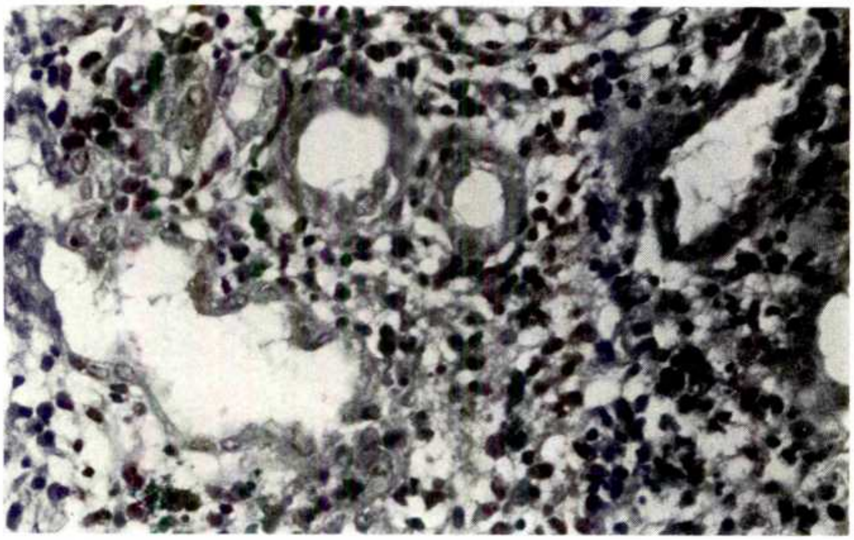


Fig. 4. Case 1. Detail of Figure 3. Tubules lined by cuboidal epithelium surrounded by lymphocytes (H&E. ×120).

Case 1. Some of the glands showed cystic dilatation being filled with mucus which was PAS-positive, diastase-resistant, and Alcian blue-positive (Fig. 6). Chronic inflammatory infiltration was more marked in the first than in the second case. In both cases the deeper layers of the wall of the bladder were oedematous, and the muscle bundles were separated by collagen fibres, and many thick-walled blood vessels were present in the lamina propria and in the muscle layers (Fig. 7).

The electron microscopic features were similar in each case.

Tubular structures were first identified in 1 μ toluidine-blue-stained sections and then localised in the electron microscope. They were lined by a single layer of cells (Fig. 8) whose basal lamina showed considerable thickening, folding and lamination. The luminal surface showed a variety of appearances but nowhere was it possible to

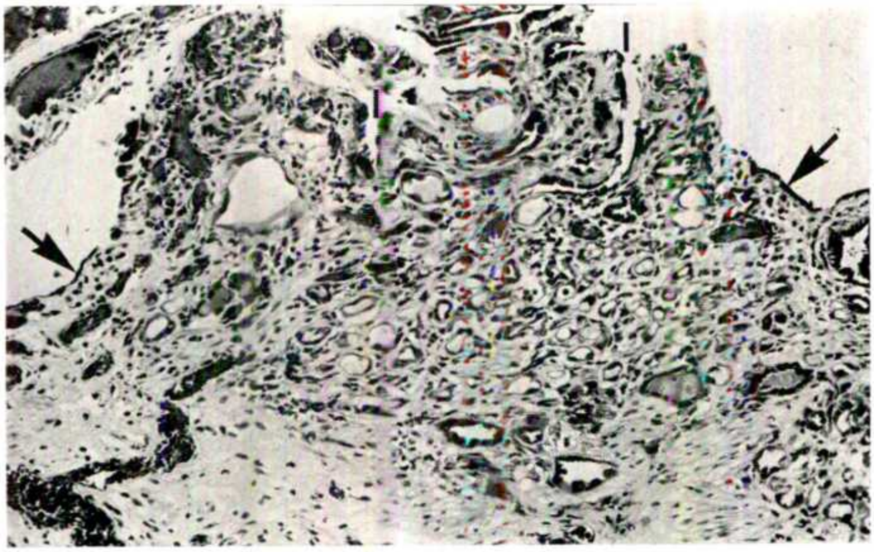


Fig. 5. Case 2. Papillary lesion showing tubules extending into the lamina propria. Some communicate with surface (I). The surface epithelium (arrowed) is lined by simple cuboidal epithelium (H&E. ×40).

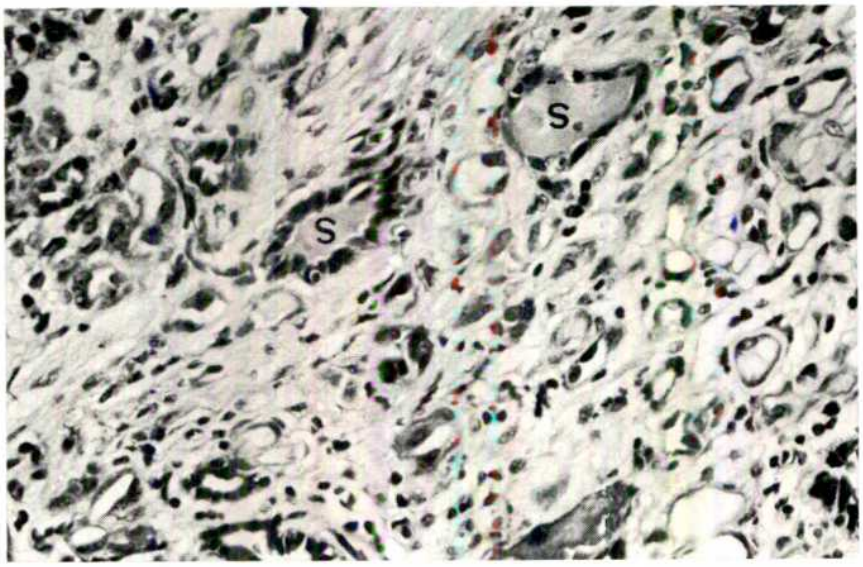


Fig. 6. Case 2. Detail of Figure 5. Secretion (S) present in some tubules: note the scanty inflammatory reaction (H&E. ×120).

identify the trilaminar asymmetrical thickened membrane which is characteristic of urothelium (Koss, 1969; Fulker, Cooper and Tanaka, 1971). Numerous microvilli were seen, coated on the luminal surface in Case 1 by a fuzz of glycocalyx beneath which lay bodies with a vesicular structure. No desmosomes were seen, but tight junctions (zona occludens) were present in the lateral cell membranes towards the luminal surface.

The nuclei of these cells were large, usually filling more than $\frac{2}{3}$ of the cell, their membranes often folded or wavy. Deep indentations or clefts on the basal aspect of the nuclei were sometimes associated with a cluster of mitochondria in the nearby cytoplasm. Nucleoli were prominent, usually in the form of a nucleolonema. Chromatin was diffuse. Mitochondria were the most prominent organelle: a few double-membrane lysosomes were also present. A Golgi apparatus with rough endoplasmic reticulum and vesicles was also seen in most cells as were microfilaments and scanty glycogen granules.

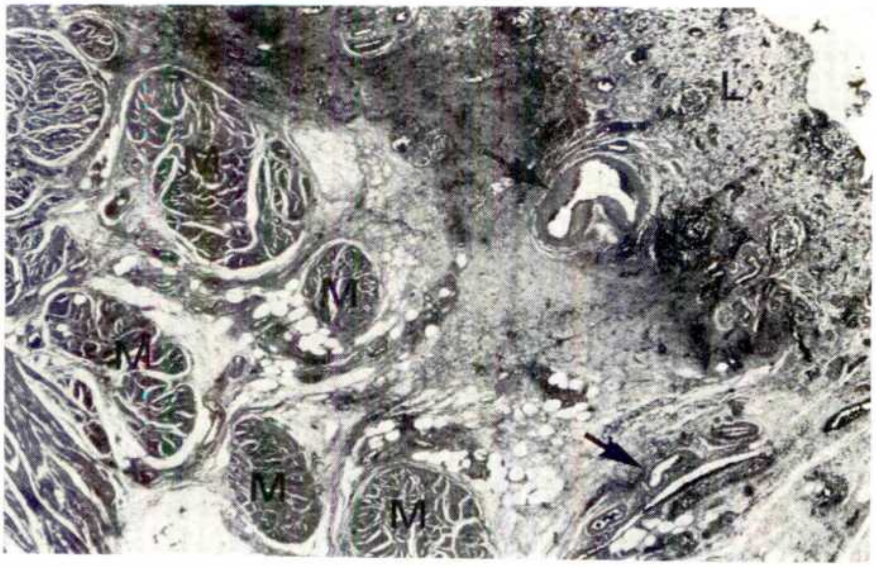


Fig. 7. Case 1. Bladder wall. Thick-walled blood vessels (arrowed) extend into the lamina propria (L). The muscle bundles (M) are divided by oedematous connective tissue and fat (H&E. × 30).

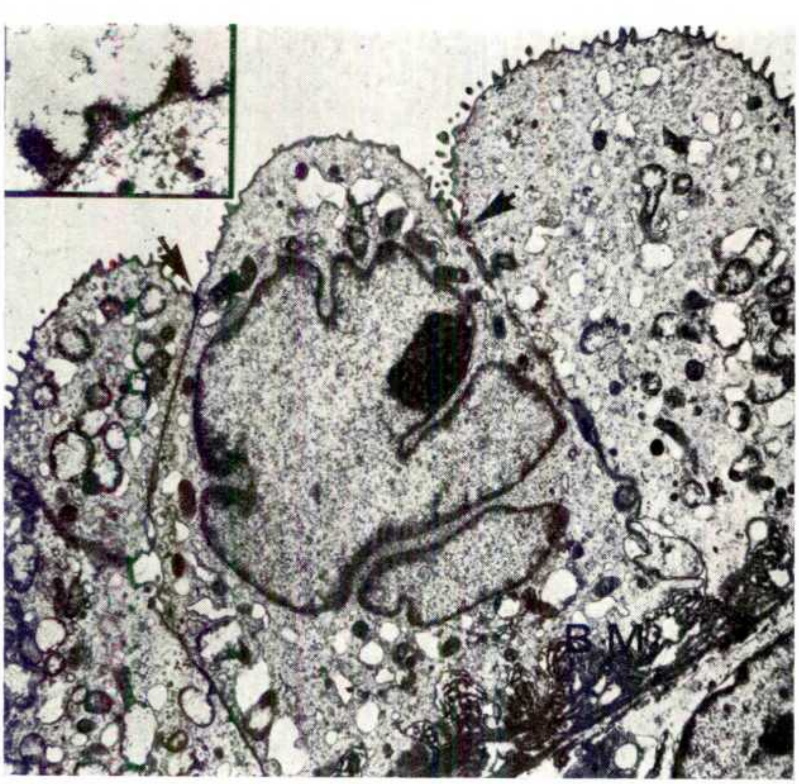


Fig. 8. Case 2. Cuboidal cells of the tubular epithelium. Tight junctions (arrowed) are visible between the cells. The nucleus is indented. The basement membrane (BM) is thickened and laminated. Inset: detail of luminal surface membrane showing microvilli with surface "fuzz". (Uranyl acetate and lead citrate × 6,500. Inset × 23,250.)

Case 3

The mucosa of the partial cystectomy specimen had reddish brown granular areas extending from the region of the trigone on to each lateral wall, with smooth-surfaced polypoidal areas in between. Microscopy showed the typical appearance of adenomatous metaplasia (Fig. 9) and immediately adjacent poorly differentiated adenocarcinoma secreting abundant mucus which had the same staining characteristics as in the previous cases being PAS positive, diastase resistant, and Alcian blue positive. The tumour was invading the wall of the bladder to the serosal surface. Some of the cystic glands in the foci of adenomatous metaplasia were lined by atypical cells and the surface epithelium which was lined by simple columnar epithelium also contained foci of atypical mucus-secreting cells. The tumour may have arisen from either of these 2 sites.

Discussion

We have reviewed our cases against the background of the 20 published reports (see Table 1), with the aim of answering 4 questions: (1) Is this truly a nephrogenic adenoma or is it a variant of urothelial metaplasia? (2) How can it be recognised? (3) Is it premalignant? and (4) How should it be treated?

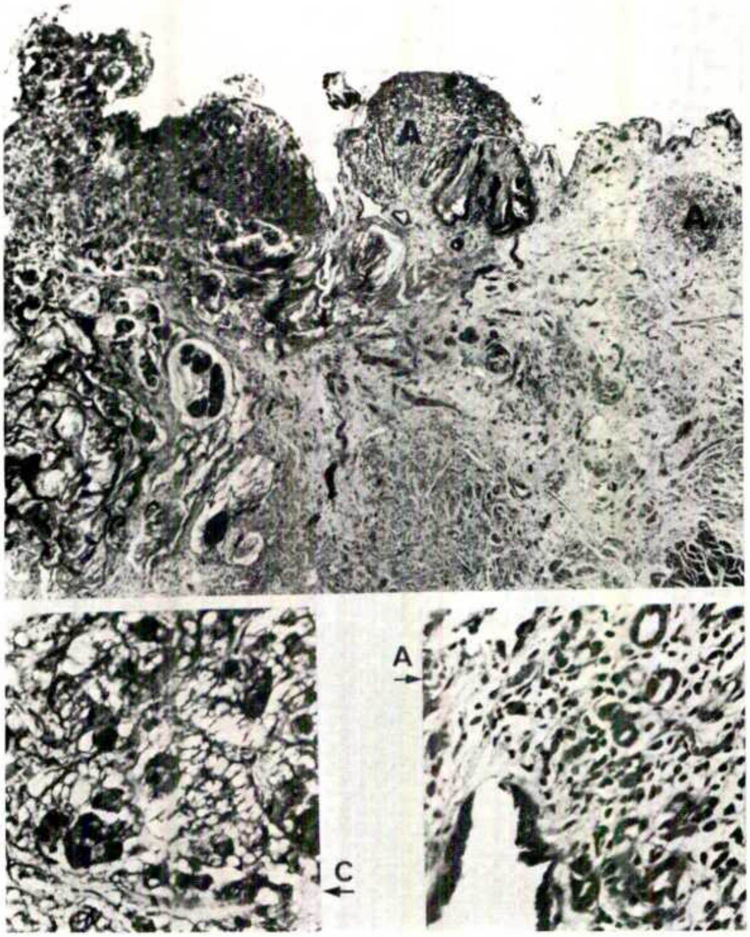


Fig. 9. Case 3. Bladder wall. Adenomatous metaplasia (M) adjacent to poorly differentiated mucin-secreting adenocarcinoma (C) which is invading muscle (lower right). (H&E. ×40.) Inset. Detail A. Adenomatous metaplasia: tubular structures, cystic dilatation. C. Carcinoma cells surrounded by mucin.

Table I

Summary of Published Reports of Nephrogenic Adenoma

Sex	Age	History	Urine	Endoscopy	Treatment	Result	Reference
M	40	backpain; dysuria, urethral discharge, haematuria	*B. friedländeri*	8 dark red granular solid lesions	TUR; antibiotics diathermy	cured	Davis (1949)
M	29	dysuria; frequency	sterile	smooth shining mass on bladder roof	antibiotics	?	Friedman and Kuhlenbeck (1950)
M	?	no data	?	polypoid tumour	?	?	Friedman and Kuhlenbeck (1950)
M	21	frequency; nocturia, haematuria	?	?	?	?	Friedman and Kuhlenbeck (1950)
M	22	frequency; nocturia; dysuria; haematuria, low back pain	sterile	resembled tuberculosis; polyps and ulcers	?	?	Friedman and Kuhlenbeck (1950
M	27	renal stone; frequency; dysuria; 3 years	?	chronic cystitis and ulcer: later "polypoid tumour"	?	?	Friedman and Kuhlenbeck (1950)
M	20	3 years dysuria and frequency	sterile on trigone	mushroom-like mass with 2 smaller masses	?	?	Friedman and Kuhlenbeck (1950)
M	25	bilateral duplex; urethral stricture; hydroureter. Haematuria 18 months	?	7 cystoscopies; 3 sessile papillomatous growths behind trigone	biopsy: diathermy	death: gangrene	Friedman and Kuhlenbeck (1950)
F	18	2 months haematuria and frequency	?	papillary tumour on posterior wall encroaching on trigone	diathermy excision	cured	Friedman and Kuhlenbeck (1950)
M	?	gunshot injury to bladder: incidental finding on cystoscopy	?	dull tumour	?	?	Holmes; cited by Mostofi (1954)
M	60	6 years before, had intraperitoneal rupture of bladder repaired with catheter drainage. Haematuria later	*E. coli* for 6 years	2 dark red mulberry lesions 1 cm diam. in bladder dome	diathermy	cured	Hasen (1962)
F	19	congenital hydronephrosis; urethral stricture; ureterolithotomy. Bilateral ureterovesicostomy; loin pain, dysuria	? ureteric orifice	flattened papillomatous tumour behind right ureteric orifice	biopsy	recurrence	Christoffersen and Møller (1972)
F	68	right nephrectomy: left renal calculi; urinary infection	?	papillomatous tumour left wall	TUR and diathermy	cure	Christoffersen and Møller (1972)
M	60	TUR: catheter: for 1 year (neuropathic bladder). Died in uraemia. Post-mortem finding	?	PM. Polypoid lesion on trigone 3 cm diameter	PM	—	Goldman (1972)
M	66	prostatitis and cystitis	?	papillary growth on trigone	TUR	?	Goldman (1972)
M	63	PM finding: stroke; indwelling catheter 1 year	?	1·5 polypoid elevation on posterior wall	PM	—	Goldman (1972)
M	16	head injury: unconscious; catheter; haematuria; dysuria. 6 months	*Proteus*	hyperaemia; 6 months later 3 small papillomatous lesions, which increased in size and number later	diathermy	improved	Kalloor and Shaw (1974)
M	23	pyelonephritis: bladder neck and diverticulum resected, nephrectomy. Dysuria 8 years. Haematuria	?	multiple papillary projections: 2-5 mm diam. on trigone and posterior wall	transvesical excision	haematuria controlled: other symptoms persisted	Taneja *et al.* (1974)
F	27	pre-eclampsia: oliguria; catheter; urethral injury; catheter. Incontinence, frequency, pain	*E. coli*	carpet-like papillary growth round left ureteric orifice	negram: diathermy	cure	Allan (1975)
M	22	loin pain; haematuria, dysuria; frequency	Gram pos cocci or sterile	non-specific chronic cystitis: later small papillary lesions posterior wall and left u.o.	antibiotics total cystectomy ileal conduit	—	Allan (1975)
M	35	renal stones; multiple operations. Gout	*E. coli* *S. faec*	brick red mucosa and patchy oedema	subtotal cystectomy and ileocaecocystoplasty	cure	Present cases
M	34	ureteric stone; Dormia basket attempted; ureterolithotomy	sterile	flat tumour round bladder neck and lateral walls	subtotal cystectomy and ileocaecocystoplasty	cure	Present cases
M	41	treated tuberculosis urinary diversion, 15 years previously	nil	polypoid and granular lesions on trigone	radical cystectomy for malignant change	recovery	Present cases

1. *Is this truly nephrogenic adenoma?*

"Nephrogenic" implies a derivation from or resemblance to renal structures. Our ultrastructural studies show that the tubules have none of the specialised features of any part of the nephron. We could find no brush border, characteristic of the proximal tubules, and none of the deep infolding of the basal membrane and the elongated mitochondria which typify the proximal and ascending thick tubules. Microvilli, fuzz on the luminal surface, and microfilaments in the cytoplasm have been described in the epithelium of the loop of Henle and of the collecting duct, but are not peculiar to these cells. On the other hand, the tubular cells lacked any of the features characteristic of urothelium such as the trilaminar surface membrane and the typical tripartite junctions (though these could have been missed by sampling error).

Our findings would support the view that these lesions represent a metaplasia of urothelium to a mesonephric-like tubule in a way which would be reminiscent of its embryological derivation from mesoderm, and adenomatous metaplasia is therefore a more appropriate name than "nephrogenic adenoma".

2. *How can it be recognised?*

The symptoms are quite non-specific, being merely those of chronic cystitis, so that the surgeon must exclude cancer, tuberculosis and bilharziasis. By now urologists have come to mistrust the cystoscopic appearances of unusual lesions in the bladder, and when in doubt, to perform multiple biopsies. In the cases described here, this was the only way the diagnosis could have been made.

3. *Is it premalignant?*

Opinions differ as to whether forms of urothelial metaplasia such as cystitis cystica and cystitis glandularis ought to be regarded as premalignant, although there is evidence that in the bladder as in other sites such changes may lead to neoplasia (Salm, 1967). Mostofi (1954) warned that carcinoma might arise in adenomatous metaplasia, and in 1 of the 2 cases reported by Christoffersen and Møller (1972) there was evidence of malignant change—acini with atypical epithelium showing signs of invasion. This appears to be the only previous case reported. Dow and Young (1968) described a case of "mesonephric adenocarcinoma" of the bladder, but their diagnosis was based on the histological resemblance to the mesonephric adenocarcinoma of the female genital tract, and there was no evidence of an origin from nephrogenic adenoma.

In 2 of our cases the severity of symptoms made it necessary to remove the bladder, but the urinary diversion in Case 3 permitted the condition to reach a state where malignancy supervened with relatively few symptoms. The evidence suggests that this change may progress to carcinoma; this consideration must influence treatment.

4. *How should it be treated?*

In 3 of the previously reported cases small patches of this lesion have apparently been cured by endoscopic diathermy, and the single example of malignant change was also cured by this method, but in a fourth case gangrene of the bladder followed and led to the death of the patient, and in the second of our cases cystodiathermy appeared only to make matters worse. Other forms of treatment are difficult to evaluate, since no follow-up is reported in 11 cases, and in 2 the diagnosis was only made *post mortem:* in 1 case only a biopsy was performed and the lesion recurred.

In our first 2 cases (as in the patient reported by Allan, 1975) the severity of the symptoms demanded cystectomy, and the bladder wall was found to be extremely oedematous and fibrotic, raising the question whether these changes might have resulted from passage of urinary solutes through a more permeable type of epithelium which had replaced the normal lining of the bladder.

Although a good result followed subtotal cystectomy and caecocystoplasty in our first 2 cases, the possibility of malignant change suggests that the remnant of epithelium at the bladder neck ought to be kept under regular endoscopic review, and that perhaps a more radical operation with an ileal conduit diversion, such as that used by Allan (1975) might be preferable, despite its effect upon the patient's sexual function.

A further question remains unanswerable on the present evidence, namely, What causes this lesion? Published accounts give no clue as to any common underlying aetiological factor though in many cases a previous operation had been performed, suggesting that perhaps pathogenic organisms had been introduced: the sporadic recovery of bacteria in the reported cases, and the variety of those isolated suggest that no common organism is likely to be responsible. Cameron (1975) informs us that "nephrogenic adenoma" is by no means uncommon, and in view of its peculiar severity, and now of the chance of malignant change, we suggest that future cases should be studied and reported in some detail, in the hope that the aetiology of this condition may be discovered.

Summary

3 additional cases of "nephrogenic adenoma" of the bladder are added to the 20 previously reported cases.

Light and electron microscopic studies of the first 2 cases support the hypothesis of urothelial metaplasia. The name "adenomatous metaplasia" should replace "nephrogenic adenoma".

Malignant change occurred in the third case, suggesting that this ought to be regarded as a potentially dangerous form of metaplasia.

In the absence of malignant change, ileocaecocystoplasty with subtotal cystectomy afforded symptomatic cure in 2 cases: radical cystectomy was performed in the third because of malignant adenocarcinoma.

References

ALLAN, E. (1975). Nephrogenic adenoma of the bladder. *Journal of Urology*, **113**, 35-41.

CAMERON, K. M. (1975). Personal communication.

CHRISTOFFERSEN, J. and MØLLER, J. E. (1972). Adenomatoid tumours of the urinary bladder. *Scandinavian Journal of Urology and Nephrology*, **6**, 295-298.

DAVIS, T. A. (1949). Hamartoma of urinary bladder. *Northwest Medicine*, **48**, 182-185.

DOW, J. A. and YOUNG, J. D. (1968). Mesonephric adenocarcinoma of the bladder. *Journal of Urology*, **100**, 466-469.

FRIEDMAN, N. B. and KUHLENBECK, H. (1950). Adenomatoid tumors of the bladder reproducing renal structures (nephrogenic adenomas). *Journal of Urology*, **64**, 657-670.

FULKER, M. J., COOPER, E. H. and TANAKA, T. (1971). Proliferation and ultrastructure of papillary transitional cell carcinoma of the human bladder. *Cancer*, **27**, 71-82.

GOLDMAN, R. L. (1972). Nephrogenic metaplasia (nephrogenic adenoma, adenomatoid tumor) of the bladder. *Journal of Urology*, **108**, 565-567.

HASEN, H. B. (1962). Nephrogenic adenoma of the bladder. *Journal of Urology*, **88**, 629-630.

KALLOOR, G. J. and SHAW, R. E. (1974). Nephrogenic adenoma of the bladder. *British Journal of Urology*, **46**, 91-95.

KOSS, L. G. (1969). The asymmetric unit membranes of the epithelium of the urinary bladder of the rat. *Laboratory Investigation*, **21**, 154-168.

MOSTOFI, F. K. (1954). Potentialities of bladder epithelium. *Journal of Urology*, **71**, 705-714.

SALM, R. (1967). Neoplasia of the bladder and cystitis cystica. *British Journal of Urology*, **39**, 67-72.

TANEJA, O. P., AURORA, A. L., GROVER, N. K., GULATI, S. M. and TAGORE, N. K. (1974). Nephrogenic adenoma of the urinary bladder. *British Journal of Urology*, **46**, 97-99.

TURNER-WARWICK, R. T. (1976). Cytoplasty. In *Urology*, vol. 2, ed. J. P. Blandy, Oxford: Blackwell, p. 841.

The Authors

E. A. Molland, MRCPath, Senior Lecturer, Department of Morbid Anatomy, The London Hospital.

P. A. Trott, MRCPath, Lecturer, Institute of Urology, London (present address: Department of Pathology Royal Marsden Hospital).

A. M. I. Paris, FRCS, Senior Registrar in Urology, The London Hospital.

J. P. Blandy, DM, MCh, FRCS, Professor of Urology, The London Hospital.

British Journal of Urology (1976), **48**, 463–467 ©

Further Studies on Effects of Irrigation Solutions on Rat Bladders

W. E. S. HARPER and L. R. MATZ

Department of Microbiology, Rehabilitation Branch of Royal Perth Hospital and Department of Pathology, Royal Perth Hospital, Perth, Western Australia

Recently we reported that irrigation of the rat bladder with an aqueous solution of chlorhexidine digluconate (1 : 5,000 and 1 : 10,000) for 6 to 48 hours usually resulted in severe erosive cystitis (Harper and Matz, 1975). However, traces of *p*-chloroaniline occur in solutions of chlorhexidine which have been autoclaved or stored for long periods of time (Martindale, 1972). In our original work we did not study the effect of *p*-chloroaniline on the rat bladder. Because of the possibility that the *p*-chloroaniline may have been partly responsible for the changes which were observed, the histological effects of this substance in the rat bladder have been investigated and are reported in this paper.

In addition, the histological effects on the rat bladder mucosa of 3 other solutions have been studied; *viz.* povidone-iodine (Betadine®) kanamycin-colistin mixture and Picloxydine®. Povidone-iodine and kanamycin-colistin were studied as they have been used as irrigating fluids in human bladders (Pearman, 1971; Lindan, 1975). Picloxydine was tested because it may prove to be a suitable bladder irrigation fluid. No oral toxic effects were observed in human volunteers using Picloxydine® mouth washes of 0·2 and 0·4% concentration (Rawal, 1976) and the antimicrobial action of picloxydine is similar to chlorhexidine (James, Baker and Wiggins, 1968).

P-chloroaniline was prepared as an 0·01% solution in distilled water or normal saline from powder of Unilab reagent grade and filtered through a Millipore® membrane (0·22 microns) and distributed aseptically in 30 ml aliquots, which were stored in a refrigerator prior to use.

Povidone-iodine in normal saline prepared aseptically by filtering through a Millipore® membrane (0·22 microns) under lamina flow conditions. A sample of the batch used was assayed for free iodine and contained 0·03% free iodine.

Kanamycin-colostin solution contained 150 mg of kanamycin base and 30 mg of Colistin base with Nipagin preservative, 0·1% W/V.

Picloxydine® solutions were prepared from Picloxydine gel which contained 5·17% Picloxydine base, (1·4 Bis-N4-p-chlorophenyl) amido amidinyl piperazine digluconate. The 0·1% solution was prepared in either distilled water or normal saline from the gel and filtered through a Millipore® membrane (0·22 microns) sealed in 30 ml aliquots and stored in a refrigerator prior to use. The concentration of Picloxydine in the final solution was 0·005% W/V (1 : 20,000).

Method of Irrigation

3-month-old Wistar male rats were anaesthetised with 22·5 mg of thiopentone in 0·5 ml of sterile distilled water injected intraperitoneally. The abdomen was surgically prepared by using 2·5% hexachlorophene soap which was rinsed with water and subsequently swabbed with 70% alcohol. A midline incision was made to expose the fundus of the bladder. The proximal attachment of a sterile Intracath® was cut to form a small cuff. This cuff was inserted into the bladder and held in position with catgut sutures. The free end of the catheter was passed through a needle which was so positioned that the catheter emerged through the skin at the base of the tail, thereby preventing the animal from damaging the catheter when it was held in a cage with its tail protruding. The needle was removed

Table I

Reaction of Rat Bladders to Irrigating Solutions

Irrigating solution	No. tests	Histological grading of reaction Mild	Moderate	Severe
Povidone/Saline (0·03% free iodine)	11	–	1	10
p-Chloroaniline/Water 0·01% W/V	11	7	3	1
p-Chloroaniline/Saline 0·01% W/V	10	5	3	2*
Picloxydine/Water 0·005% W/V	10	1	5	4
Picloxydine/Saline 0·005% W/V	13	7	4	2*
Kanamycin/Colistin/Water	13	2	1	10
Kanamycin/Colistin/Saline (150 mg Kanamycin 30 mg Colistin base with Nipagin preservative 0·1% W/V)	12	2	1	9
Distilled sterile water	11	8	3	–
Normal saline	10	8	2	–

* Clumps of *Cocci* found in bladders possibly affecting result.

and the wound closed in layers. A syringe containing 30 ml of the test solution was attached to the catheter and the injection controlled by a constant infusion pump which gave a flow rate of 1·5 ml per hour. The rats were sacrificed after 18 hours and the bladder removed immediately, fixed in 10% formol saline with 0·3 ml of the fixative also being injected through the catheter prior to placing bladder in fixative jar. The bladders were then bisected longitudinally under a dissecting microscope and 5μ paraffin embedded H.&E. sections were examined from both halves. All bladders examined appeared to have normal amount of fluid content compared with controls and macroscopically were not considered to be distended by the test solution injected. The rats had water, feed *ad libitum*, and micturated normally during the course of the experiment.

Test Series of Experiments

A total of 101 rat bladders were irrigated, and the number irrigated by each solution is indicated in Table I. A blind histological assessment was made of the bladders by L. R. M. and the changes graded according ot the criteria previously published (Harper and Matz, 1975).

Results

Table I shows the number of rat bladders irrigated, the solutions tested and histological grading. Because of the small numbers involved in the various test experiments previously published, data has been incorporated in Table II so that the antiseptic solutions can be compared with respective vehicles (water or saline) and the degradation product *p*-chloroaniline, the probability of difference by change (*p*) being established by Fisher's hypergeometric test.

The bladder changes were graded into one of the following categories:

1. Mild changes—epithelial flattening, focal superficial desquamation, cytoplasmic vacuolation, occasional mitosis, sub-mucosal oedema.

Table II

Comparison of Various Irrigating Solutions with their Respective Vehicles, Water (W) or Saline (S), with Probability of Difference by Chance (p) using Fisher's Hypergeometric Test

	Irrigating solution	Result		
		Mild–Moderate	Severe	p
Vehicle (control)	Saline (Tables I* and II)	22	2	–
	Water	10	0	–
Antiseptics	Chlorhexidine 0·02% W/V (W)*	6	12	<0·01
	Chlorohexidine 0·01% W/V (W)*	3	6	<0·01
	Povidone–iodine (0·03% free iodine) (S)	1	10	<0·01
	Kanamycin/Colistin (W)	3	10	<0·01
	Kanamycin/Colistin (S) (150 mg Kanamycin 30 mg Colistin base with Nipagin preservative 0·1% W/V)	3	9	<0·01
	Picloxydine 0·005% W/V (S)	11	2	N.S.
	Picloxydine 0·005% W/V (W)	6	4	N.S.
Degradation product	*p*-Chloroaniline 0·01% W/V (W)	8	2	N.S.
	p-Chloroaniline 0·01% W/V (S)	10	1	N.S.

* Data included from Table I of previous publication (Harper and Matz 1975).

2. Moderate changes—cellular basophilia, frequent mitoses, cellular proliferation, focal areas of mucosal desquamation, cellular swelling, with fibroblastic proliferation or mild acute inflammatory cell infiltration in the lamina propria.
3. Severe changes—mucosal erosion, inflammatory cell infiltration, fibrin precipitation, haemorrhage.

Discussion

The results indicate that *p*-chloroaniline was not a significant factor in the development of erosive cystitis in the previous chlorhexidine irrigation experiments. They are further supported by the fact that the 0·01% solution which was used in the present tests was 10 times the concentration expected in a 1 : 5,000 or 1 : 10,000 chlorhexidine digluconate solution after excess autoclaving (Martindale, 1972).

Table II also shows that the "antiseptics" kanamycin-colistin (in water or saline) and povidone-iodine (in saline) have significantly different results from their respective vehicles and are likely to be associated with erosive cystitis. However, this has not to our knowledge been clinical experience. Kanamycin-colistin solution has been used as an irrigating fluid in catheterisation procedures in the management of bladders of spinal patients at Royal Perth (Rehabilitation) Hospital, but there has been no evidence of macroscopic haematuria in over 30,000 instillations of this solution (Pearman, 1976). Similarly, Lindan (1975) has not observed macroscopic haematuria in spinal injury patients undergoing intermittent catheterisation using povidone-iodine. In other situations where povidone-iodine solutions have been used, untoward effects have not been reported (Shook, 1963; Sweeney, 1963) and Landes, Melnick and Hoffman (1970) did not report irritation after the application of povidone-iodine ointment to the urethral meatus.

It would seem therefore that the continuous irrigation procedure of the experiments with kanamycin-colistin and povidone-iodine resulting in erosive cystitis cannot be compared with the practical clinical situation. Nevertheless, the experiments have shown that these irrigating solutions can be associated with mucosal irritation. Whilst random catheterisation procedures with these fluids presumably do not have irritant effects this may not be so with repeated catheterisation. In the management of the acute phase of spinal injury patients the bladder mucosa is for 6 to 8 weeks frequently exposed to the irrigating solution after residual urine has been drained. Subclinical mucosal damage may well develop under these circumstances and clinicians should be cognisant of the potential damaging effect of these solutions. The strength of kanamycin-colistin irrigation solution used was 10 times stronger than the normal therapeutic dose usually administered. However, as it is excreted unconjugated through the kidney, further histological studies of rat bladders after a therapeutic course of these drugs singly and in combination would be of interest.

Analysis of the picloxydine results showed no significant difference between the effects of the irrigations with saline, water and Picloxydine® in terms of severe bladder changes. However, if the individual groups of mild, moderate or severe changes are assessed there is a difference between the figures for Picloxydine®, the vehicles and chlorhexidine. It appears probable that Picloxydine® affects the bladder more than the vehicles but less than chlorhexidine. As the Picloxydine® results are inconclusive, we believe further studies are required before it could be recommended for use in human bladders, particularly with respect to its bactericidal properties in urine.

Another aspect worthy of consideration is whether or not the osmolality of irrigation fluids contributed to the results. The solution *p*-chloroaniline in water had an osmolality of < 1 and in saline 282 mosmol/kg. The majority of the bladder changes were in the mild moderate group. The povidone-iodine solution in saline, however, had an osmolality of 290 mosmol/kg and most of the bladder changes were in the severe group. Kanamycin-colistin in water had an osmolality of 30 mosmol/kg, but again the majority of bladder changes were in the severe group. This would suggest that osmolality was not a significant factor in our results.

Finally, at first glance it may appear that saline caused severe bladder changes in 2 experiments. These experiments, reported in our previous paper, were complicated by the presence of bacteria in 1 case and failure of the irrigation pump in the other. This suggests that severe changes in saline irrigated rat bladders are only likely to occur if the experiments are complicated by chance infection or mechanical failure, particularly as in the second series of experiments, severe changes did not occur in saline irrigated bladders.

Summary

Further studies on the effects of certain irrigating fluids on the rat bladder for 18 hours are reported.

The results have shown that the degradation product *p*-choloroaniline is not a significant factor in chlorhexidine-digluconate associated erosive cystitis.

A high percentage of kanamycin-colistin and povidone-iodine irrigations were associated with erosive cystitis and suggested a possible complication with human usage.

Picloxydine® irrigations appeared to have a lower incidence of erosive cystitis but further studies would have to be performed before it could be recommended for use in urological procedures.

We would like to thank: Dr J. W. Pearman for his encouragement and interest, also Dr J. R. Warren for assisting with the statistical analysis, and Nicholas Pty. Ltd., 699 Warrigal Road, Chadstone, Victoria, Australia, for kindly supplying the Picloxydine Digluconate Gel.

References

HARPER, W. E. S. and MATZ, L. R. (1975). The effect of chlorhexidine irrigation of the bladder in the rat. *British Journal of Urology*, **47**, 539-543.

JAMES, J. W., BAKER, J. A. and WIGGINS, L. F. (1968). The synthesis of some heterocyclic derivatives of biguanide with antibacterial activity. *Journal of Medicinal Chemistry*, **11**, 942-945.

LANDES, R. R., MELNICK, I. and HOFFMAN, A. A. (1970). Recurrent urinary tract infections in women: prevention by topical application of antimicrobial ointment to urethral meatus. *Journal of Urology*, **104**, 749-750.

LINDAN, R. 1975). Personal communication. Chief, Infection Control Unit, Highland View Hospital, Cleveland, Ohio, USA.

MARTINDALE (1972). Chlorhexidine. *Extra Pharmacopoeia* 26th Edition. London: Pharmaceutical Press, p. 176.

PEARMAN, J. W. (1971). Prevention of urinary tract infection following spinal cord injury. *Paraplegia*, **9**, 95-104.

PEARMAN, J. W. (1976). Personal communication. Department of Microbiology, Royal Perth Hospital, Western Australia.

RAWAL, B. D. (1976). Personal communication. Department of Pharmacy, Division of Pharmaceutical Microbiology, University of Queensland, St Lucia, Australia.

SHOOK, D. M. (1963). A clinical study of a povidone-iodine regimen for resistant vaginitis. *Current Therapeutic Research*, **5**, 256-263.

SWEENEY, W. J. 1963). Perineal shaves and bladder catheterizations: necessary and benign, or unnecessary and potentially injurious? *Obstetrics and Gynecology*, **21**, 291-294.

The Authors

W. E. S. Harper, FIMLS, AAIMT, Senior Technologist in Charge.
L. R. Matz, FRCPA, Pathologist.

Requests for reprints to: W. E. S. Harper, Department of Microbiology, Rehabilitation Branch, Royal Perth Hospital, Selby Street, Shenton Park, Western Australia 6008.

British Journal of Urology (1976), **48**, 468 ©

Short Case Report

A Gynaecological Presentation of Phaeochromocytoma of the Urinary Bladder

An 11-year-old girl complained of passing blood and clot on approximately 2 days of every week. Severe haemorrhage occurred when she was 13 years old and she was admitted to a gynaecological unit. Blood was seen to come from the urethra and a mass felt in the bladder on bimanual examination. An intravenous pyelogram showed an irregular filling defect on the left side of the bladder (Fig.). Cystoscopy was performed but the view was obscured by clots. The bladder was opened and a tumour was found projecting from the left lateral wall. The tumour was excised as a limited partial cystectomy and weighed 7 g. The histological features were those of a phaeochromocytoma arising in bladder.

She went home on the 7th postoperative day and 4 weeks later a 24-hour urine collection showed a level of 0·3 mg metadrenaline per day. (Normal 1·0 mg per day.) 6 weeks after operation she began once more to pass clots. Check cystoscopy showed no evidence of residual tumour, suggesting that on this occasion, the haemorrhage was indeed menstrual. The bleeding stopped after 5 days.

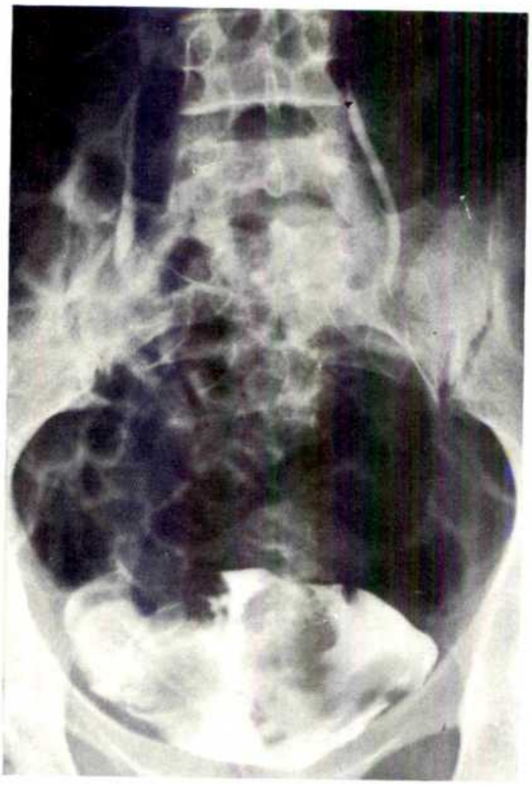


Fig. Intravenous pyelogram showing filling defect on the left side of the bladder.

Comment

The commonest position in the bladder is in the trigone. Only 7% are malignant and wedge resection with wide local margins is recommended by Leestma and Price (1971).

Usually the patient presents with the triad of hypertension, often paroxysmal, haematuria and micturition-induced attacks of throbbing headache, palpitation and sweating. The patient described here is unusual in that haemorrhage was severe to the extent of endangering life.

In most cases the urine will show an increase in metadrenalines which can persist for several weeks after removal of the tumour. However, absence of this elevation does not exclude the presence of a phaeochromocytoma or the occurrence of the classical symptoms attributed to an increase in production of adrenaline and noradrenaline (Bogaert and Vermeulen, 1972).

We thank Mr E. S. Glen for permission to publish this case and Dr R. C. B. Pugh for confirming the histological diagnosis.

A. S. Whyte and A. Dick
Southern General Hospital, Glasgow

References

Bogaert, M. D. and Vermeulen, A. (1972). Phaeochromocytoma of the urinary bladder, with inconclusive chemical and pharmacological tests. *American Journal of Medicine*, **53**, 797-800.

Leestma, J. E. and Price, E. B. (1971). Paraganglioma of the urinary bladder. *Cancer*, **28**, 1063-1073.

British Journal of Urology (1976), **48**, 469-474 ©

A Reappraisal of the Pfannenstiel Incision

DAVID A. GRIFFITHS
Royal Infirmary, Bristol

At the end of the 19th century surgeons were plagued by infected wounds and incisional hernias. Gynaecologists were particularly troubled by these problems because of the high incidence of chronic pelvic sepsis and their usual practice of approaching the pelvis through transverse muscle cutting incisions. Hermann Johann Pfannenstiel, 1862-1909, a German gynaecologist in Breslau developed an approach to the abdominal cavity which overcame some of the problems experienced at that time. Pfannenstiel's horizontally placed incision, curving over the mons pubis and separating the rectus abdominis muscles vertically, was designed to prevent incisional hernias which usually followed transverse muscle cutting incisions. Three-quarters of the 51 cases in which this approach was first used had chronic pelvic sepsis. The remaining quarter had problems with uterine tumours, ovarian swellings and ectopic pregnancies. No incisional hernias were found during the 2-year follow-up period. The reliability of Pfannenstiel's incision has stood the test of time, and modern gynaecologists continue to use this incision for pelvic operations because of good healing and cosmetic scars.

The Pfannenstiel incision has been adopted by many general and urological surgeons as a convenient approach to the bladder and prostate. Complications of this incision are minimal and wound healing and wound strength are generally very good. The alternative open surgical approach to the bladder and prostate involves a vertical abdominal incision, either midline or paramedian.

The author noted several patients returning to the follow-up out-patient department with inguinal hernias within several months of a retropubic prostatectomy through a Pfannenstiel incision. The present study was made to determine whether or not there was any difference between the postoperative morbidity of vertical or transverse incisions used for retropubic prostatectomies.

The Pfannenstiel Incision

The original description (Pfannenstiel, 1900) was given in great detail and started with incision of the skin approximately 8 to 12 cm long across the upper border of the pubic hair. This transverse incision was continued through the superficial fascia, external oblique, internal oblique, and transversalis fascia from one inferior epigastric vessel to the other. The rectus abdominis muscles were separated vertically without cutting, for 6 cm. The linea alba was cut with a knife. The next step was to lift up the transversalis fascia, pre-peritoneal fat and peritoneum, and then divide this to utilise the whole incision.

Closure of the Pfannenstiel incision was in the reverse order. Particular attention was given by Pfannenstiel to the exact and meticulous closure of the abdominal fascia (rectus sheath, and external oblique aponeurosis).

Method

The records and progress of 761 patients who had had an open prostatectomy in the United Oxford Hospitals and the Royal Devon and Exeter Hospitals during 1960 to 1965 were examined until 1974. 411 patients had transverse (Pfannenstiel) and 350 had midline or vertical abdominal

Table I

A Study of Post-retropubic Prostatectomy Inguinal Hernias

Patients from the United Oxford Hospitals and the Royal Devon and Exeter Hospitals, 1960-1965, followed up until 1974	
761	Retropubic prostatectomies
411	Transverse abdominal incisions (Pfannenstiel)
350	Vertical abdominal incisions (midline)
Associated inguinal hernias	
16	Previous inguinal hernia repairs
33	Inguinal hernias repaired at the same time as the prostatectomy
12	Inguinal hernias were left alone
Post Pfannenstiel incision inguinal hernias	
10	Inguinal hernias developed (6 right, 4 left)
3	Inguinal hernias present at the time of the prostatectomy required repair later
Post midline incision inguinal hernias	
2	Inguinal hernias developed
Incisional hernias	
2	Incisional hernias developed after transverse incisions
2	Incisional hernias developed after midline incisions

incisions. The operations were performed by a large range of surgeons and various sutures were used. The age range and symptomatology were distributed equally between the 2 groups of patients. The most common reason for the prostatectomy was acute retention due to benign hypertrophy of the prostate.

16 men had previous inguinal hernias repaired years before their prostatectomy. 33 men with inguinal hernias had had them repaired at the same time as the prostatectomy, and 12 men with asymptomatic inguinal hernias did not have them repaired at their prostatectomy.

Results

Pfannenstiel Incision

10 patients who had had Pfannenstiel incisions developed new inguinal hernias and 3 men with asymptomatic hernias and 3 men with asymptomatic hernias at the time of the prostatectomy required surgical repair because of increased symptoms shortly after their prostatectomy (Table I). One man who had a previous right inguinal hernia repaired 4 years before a retropubic prostatectomy through a Pfannenstiel incision, developed a recurrent right inguinal hernia 10 months later.

There was an equal right and left distribution in the side of new inguinal hernias following Pfannenstiel incisions (Table II). 6 inguinal hernias occurred within 1 year and a further 2 within 2 years. All the post-Pfannenstiel inguinal hernias were of the oblique or indirect form and had wide necks.

3 patients with asymptomatic inguinal hernias at the time of their prostatectomy through a Pfannenstiel incision, returned for surgical repair at 1, 2 and 3 years respectively, with increased symptoms of discomfort, swelling and dragging pains.

Midline Incision

2 men out of the 350 who had prostatectomies through midline incisions developed inguinal

Table II

Post-Pfannenstiel Incision Inguinal Hernias

Name	Age	Type	Side	Time after prostatectomy
W. T.	84	Ind.	RIH	immediately
A. B.	79	Ind.	LIH	5 months
C. C.	82	Ind.	LIH	6 months
W. G.	84	Ind.	LIH	12 months
H. P.	64	Ind.	RIH	12 months
G. L.	70	Ind.	RIH	12 months
H. G.	61	Ind.	LIH	18 months
H. H.	69	Ind.	RIH	24 months
C. W.	79	Ind.	RIH	6 years
P. B.	74	Ind.	RIH	6 years
Inguinal hernias present before prostatectomy which required surgical repair later				
W. G.	79	Ind.	LIH	12 months
C. C.	69	Ind.	RIH	24 months
H. A.	74	Ind.	Bil.	36 months

hernias at 1 and 9 years later. 9 men with asymptomatic inguinal hernias at the time of their prostatectomy through a vertical incision remained asymptomatic and did not require repair.

Incisional Hernias following Prostatectomy

There was an equal distribution of incisional hernias between the 2 groups. 4 incisional hernias developed, all following infected wounds; 2 of these came on after midline incisions and 2 after Pfannenstiel incision.

Significance

From the above results it is seen that there was an increased incidence of inguinal hernias following Pfannenstiel incisions in men. At the 2-year follow-up period there were 8 inguinal hernias following Pfannenstiel incisions and 1 following the midline incision. For this period, Fisher's "Exact Probability Test" gave $P = 0{\cdot}028$, which is significant when comparing a real difference between the 2 groups.

Discussion

The significant increased incidence of inguinal hernias following Pfannenstiel incisions in men compared with vertical abdominal incisions has been proved in this study. The reasons for this and the possible mechanism will be discussed. The possible reasons are (1) nerve injury, (2) increased intra-abdominal pressure and (3) weakening of the inguinal canal.

1. *Nerve Injury*

No motor nerves should be injured by the classical Pfannenstiel incision as most of the incision is anterior to the neurovascular plane and runs parallel to the neurovascular bundles, without reaching the fleshy parts of the muscle.

2. *Increased Intra-abdominal Pressure*

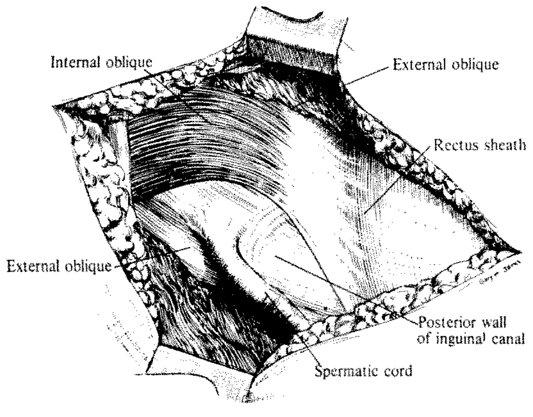
Outflow obstruction of the bladder with increased intra-abdominal pressure during micturition has been sometimes mentioned as a factor in hernia formation. The probable significance of intra-abdominal pressure as a cause of inguinal herniation is controversial. In the present study the outflow obstruction has been relieved by the prostatectomy and any increased intra-abdominal pressure would have played an equal part in both midline and transverse incision prostatectomies.

3. *Weakening of the Inguinal Wall*

The posterior wall of the inguinal canal plays an important part (Fig. 1) in preventing the development of inguinal hernias. The lower border of the transverse abdominis layer forms a curved line, the transversus abdominis arch. This arch forms the superior border of most inguinal hernias (Anson, Morgan and McVay, 1960). In 68% of normal groin dissections, they found that the arching line was at least 0·5 cm but less than 2 cm above the superior ramus of the pubis. Their description of the ideal hernia-proof disposition of the lowermost fibres of the internal oblique and transversus abdominis was a shallow arch extending as low as the pubic tubercle, so that the muscle can act as a shutter or sphincter when it contracts. In 8% of normal inguinal regions they found that there were arching fibres of the internal oblique inserted well above the pubic tubercle, thereby making it impossible to exert the protective shutter or sphincter action on exertion. They concluded that this deficiency would be one of the factors predisposing to hernia formation. The protective layer of the transversalis fascia varies considerably; in 20% of their dissections they judged this fascia to be of insufficient strength to support the inguinal region against a moderate strain. These facts have been known and used by surgeons for many years. Numerous methods of strengthening the posterior wall of the inguinal canal have been devised. Tanner (1942) described a method to strengthen the posterior wall with the lateral rectus sheath. A curved incision (Fig. 2) in the anterior rectus sheath over the muscle, relaxed the fascia enabling the surgeon to suture it to the inguinal ligament. This closes the gap through which inguinal hernias can develop. I examined and repaired 6 cases of inguinal hernia following Pfannenstiel incision, and 1 case of a recurrent inguinal hernia. All of these hernias were indirect in that they came out laterally to the inferior epigastric vessels and not through Hesselbach's triangle. However, there was a marked arching lower border of the internal oblique and transversus abdominis. This arching is often seen in straightforward hernias, but in these the border and muscles are mobile. When the hernial sac is reduced in the normal inguinal hernia there is some attempt by the surrounding muscles to bridge the gap. In the inguinal hernias I have examined that appeared following Pfannenstiel incision, this mobility of the muscles was lost. The whole of the transversus abdominis arch was fibrotic and remained rigid during reduction and excision of the hernial sac. The reason for this was that the previous Pfannenstiel incision had entered the upper reaches of the inguinal canal, and the healed incision had scarred the muscles. There was also a marked increase in the critical area of the posterior inguinal wall. This appeared to be due to the hitching up of the inferior border of the aponeurosis of the internal oblique and transversus abdominis. These changes were not thought to be due to the hernial sac, but brought about by contraction of the earlier, healing sutured Pfannenstiel incision just slightly higher in the abdominal wall (Fig. 3).

This mechanism which produces weakness in the posterior inguinal wall can be compared or likened to a reversed Tanner slide. The upward slide would be emphasised by incorrect and over-tightened sutures in the Pfannenstiel incision. Tanner mentioned that damage to the lower rectus sheath and muscles by previous operation precluded the use of slide operations for inguinal hernia repair.

The original description by Pfannenstiel gave emphasis and warning not to extend the incision too far laterally. The wider use of the Pfannenstiel incision has meant that it has been altered and changed into something little resembling the original description. The inadvertent extra extension of the Pfannenstiel incision into the superior region of the inguinal canal means that when sutured, the inferior border of the aponeurosis of the internal oblique and transverse abdominis will be elevated. This occurs when the sutures are tied, especially if they are widely placed and over-tightened. This effect is compounded by contraction of the healing fibrosed scar tissue. The muscle shutter mechanism is destroyed, and the angular defect between the lateral border of the rectus



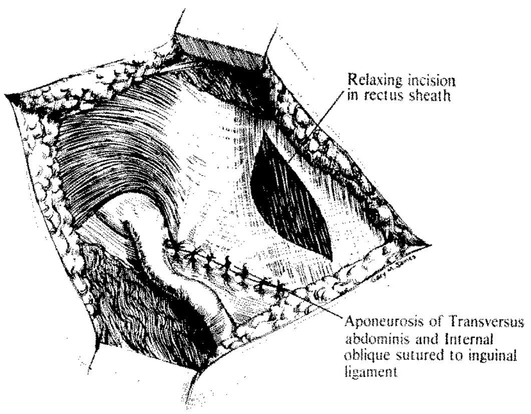

Relaxing incision in rectus sheath
Aponeurosis of Transversus abdominis and Internal oblique sutured to inguinal ligament

Fig. 1 (left). The normal inguinal canal. The external oblique aponeurosis has been incised and the contents of the canal exposed. The spermatic cord passes through the inguinal canal from the deep inguinal ring to the superficial inguinal ring.

Fig. 2 (right). "Tanner slide." A relaxing incision has been made in the rectus sheath and the posterior wall of the inguinal canal has been strengthened by suturing the lateral border of the rectus sheath to the deep part of the inguinal ligament.

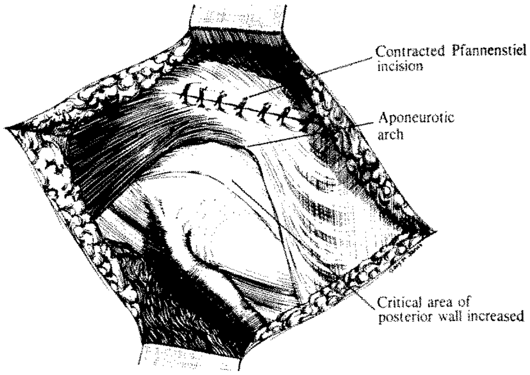

Contracted Pfannenstiel incision
Aponeurotic arch
Critical area of posterior wall increased

Fig. 3. The posterior wall of the inguinal canal has been weakened by the arching upwards of the internal oblique and transverse abdominus. The "Pfannenstiel incision" wound can be seen in the upper border of the inguinal canal.

sheath and the inguinal ligament is increased. The strength of the posterior wall is left to the transversalis fascia, and as mentioned before, this is very variable. If the transversalis fascia is weak, an inguinal hernia is likely to develop (Anson and McVay, 1971).

Conclusion

The Pfannenstiel incision produced a significant increase in the incidence of indirect inguinal hernias following prostatectomy. The mechanism for this was thought to be due to injury and changes in the architecture of the inguinal canal. Following Pfannenstiel's original description in all its detail would avoid this. There appeared to be no significant morbidity in using the midline vertical incision for retropubic prostatectomy and it has an added advantage of avoiding the elderly inguinal canal.

The second result from this study showed that men in their 80s with asymptomatic inguinal hernias at the time of prostatectomy returned years later for surgical correction. It would seem appropriate that, other things being equal, concomitant hernias should be repaired at the same time as the prostatectomy.

Summary

The postoperative morbidity of incisions used in retropubic prostatectomies was examined. 350 patients with vertical midline incisions were compared with 411 patients with transverse or Pfannenstiel incisions.

There was a significantly increased incidence of postoperative inguinal hernias in the group of patients who had had transverse incisions. The possible reasons for this were discussed.

It was concluded that the normal architecture of the inguinal canal was deformed and weakened by extra-wide transverse incisions.

I would like to thank past and present surgeons of the United Oxford Hospitals, and the Royal Devon and Exeter Hospitals for allowing me to include details of patients under their care.

References

ANSON, B. J., MORGAN, E. H. and MCVAY, C. B. (1960). Surgical anatomy of the inguinal region based upon a study of 500 body-halves. *Surgery, Gynecology and Obstetrics*, **111**, 707-725.

ANSON, B. J. and MCVAY, C. B. (1971). *Surgical Anatomy*, 5th ed. Philadelphia, Saunders, p. 489

PFANNENSTIEL, J. (1900). Über die Vortheile des suprasymphysären Fascienquerschnitts für die gynäkologischen Koliotomien, zugleich ein Beitrag zu der Indikationsstellung der Operationswege. *Sammlung Klinische Vortrage* **268**, 1736-1755.

TANNER, N. C. (1942). A "slide" operation for inguinal and femoral hernia. *British Journal of Surgery*, **29**, 285-289.

The Author

David A. Griffiths, MD, FRCS, FRCSE, Senior Surgical Registrar (now Consultant Surgeon, Yeovil District Hospital, Yeovil, Somerset).

British Journal of Urology (1976), **48**, 475-477 ©

Live Television Transmission of Transurethral and Open Pelvic Surgery with Reproduction on a Big Screen

E. ZINGG, R. TSCHOLL and K. STIEF
Urological Department of the University of Berne and Maurice Müller Foundation Berne

Mammoth congresses with an unlimited number of participants may serve a social purpose. For demonstrating and comparing surgical procedures small workshops attended only by experts are much more rewarding.

Workshops concerning operative techniques can be based on recorded surgery stored on film and video tape or on live television transmission.

Recorded surgery has the advantage of showing carefully planned purified typical operations performed without unforeseen incidents. Important steps may be emphasised and elaborated upon in such a way that the recording is valuable for beginners.

As time consuming and "uninteresting" difficulties are usually cut out the beginner's advantage turns into a serious drawback for surgeons who have already done the operation themselves and who may have encountered repeatedly the same technical problem. That is why experts will be interested in discussing and comparing step by step their own technique with the one being demonstrated. Discussion with the operating surgeon is not of course available from recorded surgery but television-covered surgery is the ideal means for providing individually sought information: the audience may ask questions during the operation and the surgeon can demonstrate specific details which might otherwise remain unclear.

The television picture can be visualised on conventional colour monitors or by the Eidophor system on a big screen with a surface area of 12 m^2, the actual image covering 6 m^2.

The purpose of this paper is to introduce a method which makes it possible to show, by direct television transmission on a big screen, (1) open surgery in the depth of the pelvis where the visibility even for the assistant is often hampered and, (2) transurethral surgery.

Method

Television cameras LDM I Phillips were used. A complete almost professional television network allowed video and sound mixing. The operating theatre, the studio and the auditorium were in permanent speaking communication over a distance of more than 600 m. The light was derived from a xenon high pressure cold light fountain with a 500 watt lamp (Storz 494 F 6000) the maximal performance of which amounted to 30,000 lux.

Open Surgery

The television camera is mounted on a low cart running on top of a steel scaffold. It is thus positioned in the midline directly above the pelvis and can be pointed into any direction (Fig. 1). To allow free play to the camera the conventional operation lamp is removed and replaced by two small sterilised lamps (type Lübke Storz 500) fixed to the operation table (Fig. 2). They are supplied by the light fountain mentioned above. Any surgery even in the depth of the pelvis can be visualised. (The first operation shown was a total cysto-vesiculo-prostatectomy for bladder cancer.)

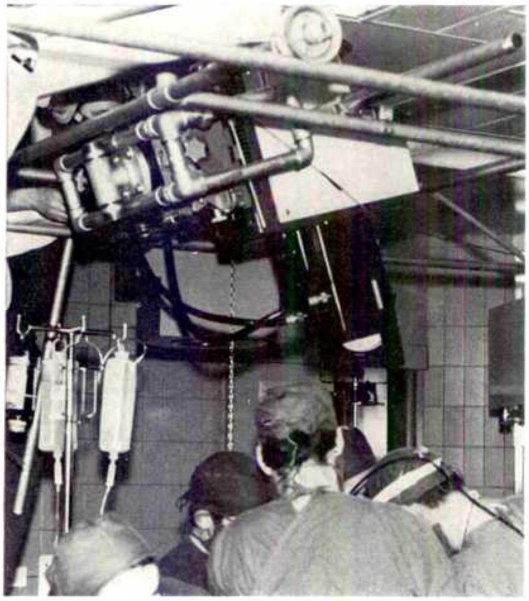


Fig. 1

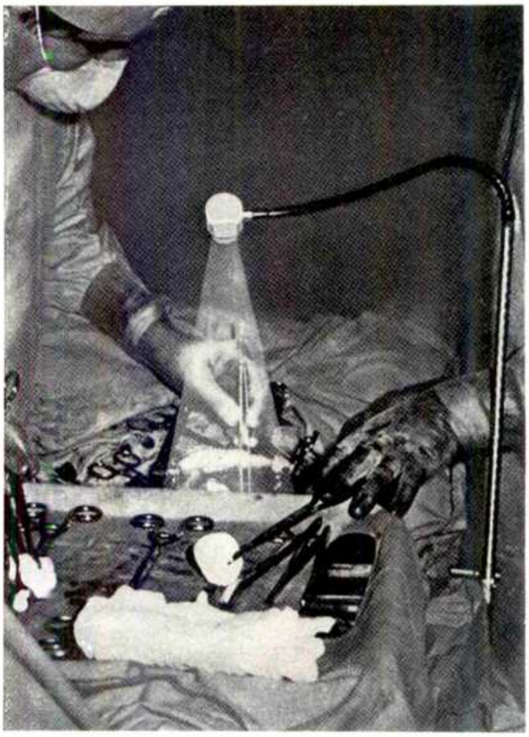


Fig. 2

Transurethral Surgery

The resections can be done with any resectoscope providing a good view. We use a Storz resectoscope. The light is brought to the telescope via a y-shaped fibre optic light cable (Storz 495 AD) which doubles the illumination.

The transmission of the endoscopic picture from the telescope to the object lens of the television camera is achieved by a jointed image transmitter, that was introduced into endoscopy by Wittmoser in Germany and perfected by Hopkins in England to the point where only a small fraction of the light is lost. The cutting and coagulating currents are produced by a Siemens electro-surgical unit Hmtg 95/3183. It is positioned in an adjoining room, which turned out to be the only practical way of screening the television camera and avoiding disturbing noises in the image.

Results and Conclusion

An optimal transmission and enlargement of the television image can be achieved by the system used. No detail is lost in the reproduction of the image on the Eidophor big screen. The camera has the same view as the operating surgeon. The spectator in the auditorium can see the whole procedure better than the assistant (Fig. 3). This cannot be achieved by a camera on a high tripod standing behind the surgeon but only by a camera practically hanging in mid-air above the surgeon.

The image of the transurethral operations (Fig. 4) seems to be gigantic. Minute details of the tissue structure which are usually overlooked are reproduced with amazing sharpness. In spite of

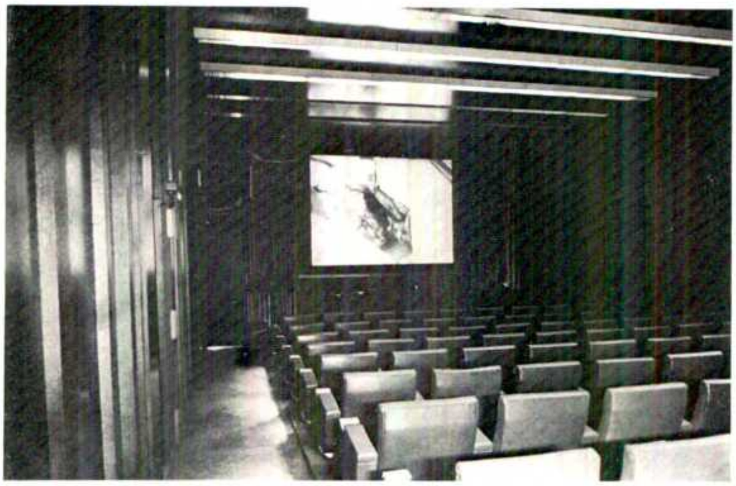


Fig. 3

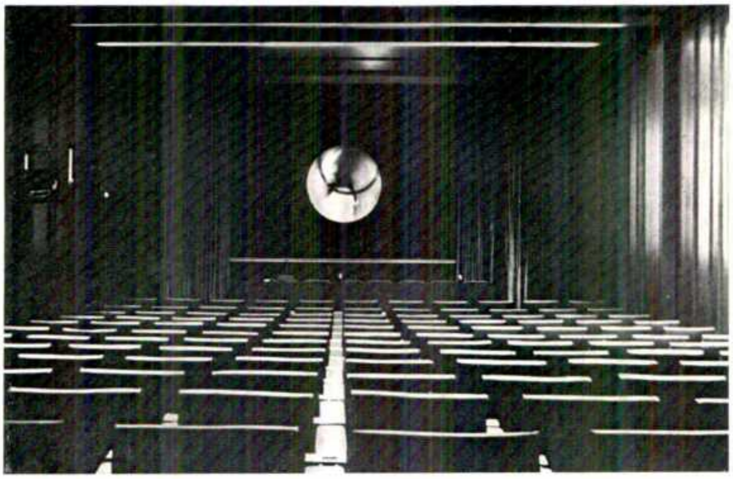


Fig. 4

the magnificent visibility of the details the view of the whole and the spectator's orientation are retained.

To our knowledge the first live television transmission of transurethral prostate and bladder surgery which could be reproduced on a big screen took place in Berne in March 1975. The procedure is now in use during workshops for postgraduate training.

We wish to thank Mr O. Keel and Mr J. Küfer for their technical help and for constructing the scaffold carrying the TV-camera.

The Authors

E. Zingg, MD, Professor of Urology.
R. Tscholl, MD, Chief Registrar.
K. Stief, Chief TV Technician, MM Foundation.

British Journal of Urology (1976), **48**, 478 ©

Short Case Report

Urinary Retention due to Congenital Posterior Urethral Polyp in a Boy

Urinary retention caused by congenital urethral polyp is a rare but well defined entity in childhood. Few and isolated cases have been reported (Braun, 1975; Juskiewensky *et al.*, 1972). A new case is communicated herein.

A 4-year-old boy was admitted in February 1973 because of inability to void, requiring continuous bladder catheterisation over a period of 1 month before admission. On several attempts at removal of the catheter, he had failed to regain spontaneous micturition. He complained of several episodes of urinary difficulty for the previous 2 years which had been misinterpreted. Urography showed a mobile filling defect at the bladder neck (Fig. 1). Cystourethroscopy disclosed what seemed a polyp arising from the base of the prostatic urethra obstructing the vesical outlet. A transvesical suprapubic excision was followed by an uneventful recovery. Histology revealed a benign polyp with a fibrovascular stroma lined by normal transitional epithelium (Fig. 2). There were scattered foci of lymphocytes. Postoperative micturition is good with sterile urine.

Posterior urethral polyp must be kept in mind whenever other causes of dysuria in boys have been ruled out. Voiding cystourethrogram and cystoscopy will give the diagnosis. In our opinion a supravesical approach is recommended avoiding endoscopic procedures. The prognosis is excellent.

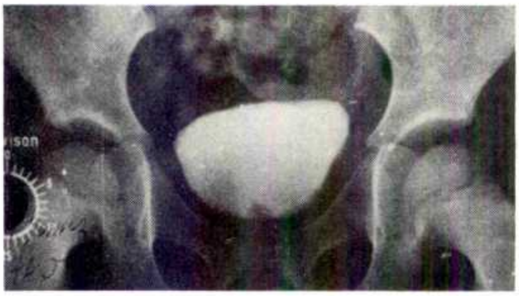


Fig. 1

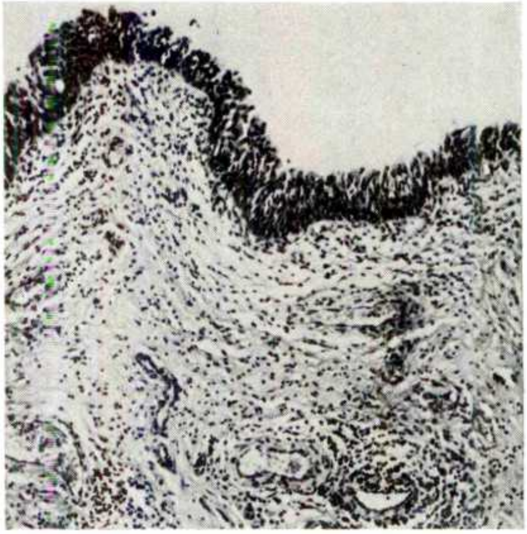


Fig. 2. H. & E. × 100.

A. Ifiéns Aznar and J. M. Martinez-Peñuela V
Departments of Urology and Pathology, Hospital de Navarra, Pamplona, Spain

References

Braun, E. W. (1975). Congenital polyp of the prostatic urethra in a child. *Journal of Urology*, **114**, 311-312.

Juskiewensky, S. *et al.* (1972). Polypes de l'urètre postérieure chez le garçon: à propos de 3 observations. *Annales d'Urologie*, **6**, 259-264.

British Journal of Urology (1976), **48**, 479–484 ©

The Value of Prophylactic Antibiotics in Transurethral Prostatic Resection: a Controlled Trial, with Observations on the Origin of Postoperative Infection

MICHAEL J. MORRIS, DAVID GOLOVSKY, MICHAEL D. G. GUINNESS and P. O. MAHER
Departments of Surgery, Urology and Microbiology, Repatriation General Hospital, Concord, N.S.W., Australia

Urinary tract endoscopy has two important infective sequelae: bacteraemia and urinary infection.

The origin of micro-organisms that enter the blood stream during endoscopic procedures has been variably blamed on urethral flora (Scott, 1929), bacteria colonising prostatic ducts and glands (Kidd and Burnside, 1965) or contamination of irrigating fluids (Last, Harbison and Marsh, 1966).

It is difficult to isolate bacteria from expressed prostatic secretions, perhaps due to anatomical factors (Blacklock, 1974) or bacteriocidal properties of fluid (Meares and Stamey, 1968) and even harder to prove that such bacteria actually come from the prostate (Murnaghan *et al.*, 1974).

However, in 1918 Rosen showed that pathogenic bacteria could be cultured from the interior of prostatic adenomata in 36% of cases, even after immersion for 20 sec in oil at 180°C to kill all surface organisms. More recently (Smart and Jenkins, 1973) confirmed that culture of prostatic chips gives a better yield of organisms than expressed secretion from the same patient.

Catheterisation bears the brunt of blame for the development of postoperative urinary tract infection (Symes *et al.*, 1972). Whether the catheter or those that handle it are culpable is a significant issue; but there is little doubt that the incidence of bacteriuria increases the longer the catheter remains *in situ.*

Infection is thus often unavoidable during and after transurethral prostatic resection (Miller *et al.*, 1958). To increase host resistance maximally to invading bacteria it is necessary to have an adequate concentration of antibiotic already in the tissue when bacteria arrive (Burke, 1963). However, the use of prophylactic antibiotics is certainly controversial (Creevy and Feeny, 1954; Plorde *et al.*, 1965; Genster and Madsen, 1970; Wear and Haley, 1973).

In this trial broad spectrum antibiotics were given prior to and following surgery in an attempt to prevent bacteraemia and postoperative urinary tract infection. Parameters examined were blood cultures, culture of prostatic chips, repeated urine cultures and tabulation of postoperative febrile episodes.

Methods

Patient Selection

101 patients at Repatriation General Hospital (Concord) underwent transurethral resection for prostatic obstruction. Only patients with a sterile preoperative and operative urine specimen were included in this study. Any antibiotic administration in the week prior to surgery resulted in exclusion from the trial. Patients were randomly assigned to either the antibiotic or control group according to their odd or even hospital number.

Table I

Age of Patient and Amount of Tissue Resected

	Control group		Antibiotic group	
	Mean	S.D.	Mean	S.D.
Age of patient (years)	70·3	±8·4	72·1	±8·5
Weight of resected prostate (grams)	15·3	±11·6	15·6	±10·4

The antibiotic group were given Kanamycin 1 g intramuscularly with their premedication or following endoscopic assessment prior to resection. Cotrimoxazole (2 tablets twice daily) was continued for 3 weeks after surgery. Antibiotics were only given to the control group (at the discretion of the resident staff) when clinically indicated by postoperative infective episodes.

Antiseptic Technique

In both groups, postoperative catheters were inserted aseptically in theatre, and closed bladder drainage was maintained.

Irrigation was by the closed intermittent method, using a Y-connection.

Penile dressings with Hibitane cream were utilised routinely and catheters were removed as soon as bleeding ceased to be a problem, generally 2 to 3 days.

Blood Cultures

These were performed during the resection and approximately 2 hours after surgery. Further blood cultures were taken during any subsequent febrile episodes.

Cultures were considered positive only if the same organism was recovered from both bottles or from consecutive sets.

Prostatic Culture

2 chips were taken from a deep portion of the gland, collected separately and sent to the microbiology laboratory in a sterile container. There they were ground aseptically and cultured in meat broth overnight, then subcultured on to blood agar and McConkey's agar.

Urine Specimens

These were collected after removal of the catheter, again prior to discharge, and at follow-up.

Urine was deemed infected when there was greater than 100,000 organisms per ml or there was repeated pure culture of the same organism. Pyuria was not included in the criteria for diagnosis of infection because of the inevitable presence of white cells in the urine following surgery.

Intermittent checks were made on the sterility of irrigating fluids and endoscopic instruments during the trial and these were always found to be sterile.

Results

Statistical comparison of both control and antibiotic groups showed them to be comparable on the grounds of age of patient, weight of tissue resected, and participating surgeons (Table I). 12 patients had carcinoma of the prostate, 6 in each group.

Of the initial 56 in the control group, and the 45 who received prophylactic antibiotics, 3 were excluded from each group because of infected urine at endoscopy.

Blood Cultures

These were positive on 10 occasions, with 4 in the antibiotic group and 6 in the control. The same organism was recovered from the prostate in 6 cases (60%).

Despite positive blood cultures clinical manifestations of Gram-negative septicaemia only occurred in 4 patients. 3 of these were in patients not covered by antibiotics.

Table II

Organisms cultured from Resected Prostate (Both Groups)

Organism	No. of cultures	% of total
Coag. +ve *staph.*	16	22
Coag. −ve. *staph*	14	19
Strep. faecalis	11	15
E. coli	8	11
Strep. viridans	8	11
Proteus sp.	6	8
Pseudomonas sp.	4	6
Non-haem. strep.	3	4
Beta haem. strep.	1	1
Bacillus sp.	2	3

Of 86 prostatic cultures, 60 grew at least 1 organism, 26 were sterile. Where operative UTI was present, prostatic culture was not included. A number of prostatic chips grew 2 different organisms.

Prostatic Cultures

These were positive in 60 cases (64%), with equal distribution between antibiotic and control group. In 10 cases 2 or more organisms were cultured (Table II).

Urine Culturse

Table III shows the organisms cultured from the urine. *E. coli* was most frequently cultured being present in 35% of cases, followed by *Strep. faecalis* in 19%, *Proteus* 19% and coagulase positive *Staph.* in 12%. 14 (26%) of the control group developed urinary tract infection in the postoperative period as against only 2 (5%) of those given antibiotics. This was statistically significant ($P < 0{\cdot}01$) (Fig. 1).

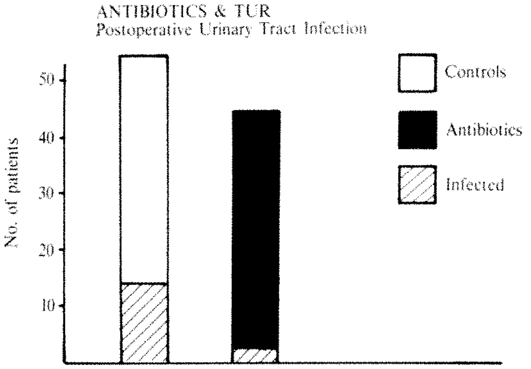
In studying the relationship between prostatic infection and subsequent urinary tract infection we will focus our attention on the control group because of the negligible incidence of urinary infection with the antibiotic group.

Of the 14 patients in the control group, 7 (50%) grew the same organism that was isolated from their prostate gland; 4 grew no prostatic organisms.

The effect of antibiotics is summarized in Table IV.

Postoperative fever

Fever greater than 38°C was equally common in each group, developing in 25 (50%) of the controls and 25 (56%) of the antibiotic group. Its occurrence also did not correlate with the development of postoperative urinary infection, and its cause remains uncertain (Fig. 2).



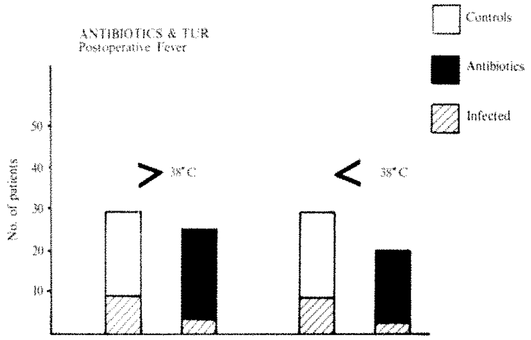


Fig. 1 (left). Comparison of occurrence of post-TUR urinary tract infection in control and antibiotic groups ($P < 0{\cdot}01$). Those cases with bacteriuria on endoscopy are included in this figure.

Fig. 2 (right). Incidence of urinary tract infection and fever compared in control and antibiotic groups. Difference significant to P less than 0·01.

Table III

Significant Organisms cultured from the Urine (Both Groups)

Organism	Frequency of culture No.	Frequency of culture %	Sensitivity to prophylactic antibiotics No.	Sensitivity to prophylactic antibiotics %
E. coli	9	35	8	89
Strep. faecalis	5	19	1	20
Proteus sp.	5	19	4	85
Pseudomonas sp.	1	4	0	0
Coag. +ve *staph.*	3	12	3	100
Coag. −ve *staph.*	1	4	1	100
Beta'haem. strep.	1	4	1	100
Enterobacter sp.	1	4	1	100

Total includes several combined infections.

Table IV

Summary of Results

	Positive prostatic culture	Positive blood culture	Positive urine culture
Antibiotic group 42 patients	28 (67%)	4 (10%)	2 (5%)
Control group 53 patients	32 (60%)	6 (11%)	14 (26%)

Discussion

The sources of urinary tract infection following surgery on the prostate are certainly multifocal in origin. Reduction in the rate of infection can be achieved by careful management of catheter drainage, minimal catheterisation time and judicious aseptic irrigation only when drainage problems are encountered (Symes *et al.*, 1972).

The normal anterior urethral flora is the same as the perineum, i.e. faecal flora and coagulase positive *Staph.* If these organisms do colonise prostatic ducts and glands they are potential foci of infection which make contamination of the operative field unavoidable.

The rate of recovery of pathogenic organisms from the prostate is certainly very high in this series. However, most authors who have cultured prostates have always recovered a significant number of bacteria. (Rosen, 1919; Kidd and Burnside, 1965; Schmidt and Patterson, 1966; Smart and Jenkins, 1973). Culture of expressed prostatic secretion on the other hand is either sterile or gives a low yield of micro-organisms.

It is possible that the prostatic chips could have been contaminated by urethral organisms or irrigating fluid prior to culture. The former is difficult to exclude but the prostate biopsies were taken from a deep portion of the gland farthest from the urethra and after significant irrigation time. In the presence of a sterile urine this is probably an insignificant cause. Irrigating fluids were cultured from time to time and were always sterile.

The frequency of reappearance of prostatic organisms in both blood cultures (60%) and postoperative urinary tract infection (50%) suggests a possible cause and effect relationship. This may be restated to the effect that where prostatic culture was positive and the urine subsequently became infected, the organism was the same in 70% of cases.

Bacteraemia occurred in 10% of the patients with initially sterile urine. By contrast 50% of the patients with an infected urine on endoscopy (later excluded from the trial) grew the same organism from the blood culture. These figures are almost identical to those of Creevy and Feeny (1954). Because of the nature of the operation and the opening of vascular channels, organisms can easily be washed into the blood stream. What is surprising is that recovery of organisms from the blood stream is the same whether or not antibiotics were administered.

Fever is common in the postoperative period. It occurs despite antibiotic cover and is unrelated to subsequent development of urinary infection. Biorn, Browning and Thompson (1950) suggest fever is unrelated to bacteraemia. Creevy and Feeny (1954) discuss the probable absorption of toxins from denatured tissue entering the circulation with the irrigating fluids. Wear and Haley (1973) suggest resection causes an excessive histamine release because of exaggerated antigen–antibody reaction in the already sensitised patient. Both are possible causes, as febrile episodes without rigors or hypotension most often settled in the first 24 hours without any specific treatment.

The question still remains as to whether prophylactic antibiotics are useful in endoscopic surgery. It appears that postoperative urinary tract infection is reduced significantly although it must be noted that infection was only encountered in 26% of those without antibiotic cover. This figure was reduced to 5% with antibiotics. The effect this reduction in urinary tract infection had on patients' morbidity is much more difficult to quantify, and must be weighed against the cost and side effects of the antibiotics. There is an argument that any infection that develops should be treated on its merits according to drug sensitivities (Genster and Madsen, 1970).

There is no evidence in this trial that the patient is protected against Gram-negative septicaemia and its associated morbidity. It is undisputed however, that, if a urinary tract infection is present prior to surgery, it must first be treated effectively because the risk of a bacteraemia increases five-fold and postoperative infection becomes inevitable.

Summary

Prophylactic antibiotics significantly decrease the incidence of urinary tract infection following endoscopic prostate resection.

They are ineffective in reducing the incidence of postoperative fevers, or in reducing the frequency of positive blood cultures during or after operation.

A majority of prostate glands harbour colonies of potentially pathogenic organisms, and these are the commonest source of infection of the urinary tract following release by prostatic surgery.

The assistance of Sister Heather Lye in collecting data contained in this paper is gratefully acknowledged.

References

BIORN, C. L., BROWNING, W. H. and THOMPSON, L. (1950). Transient bacteremia immediately following transurethral prostatic resection. *Journal of Urology*, **63**, 155-161.

BLACKLOCK, N. J. (1974). Anatomical factors in prostatitis. *British Journal of Urology*, **46**, 47-54.

BURKE, J. F. (1963). Preoperative antibiotics. *Surgical Clinics of North America*, **43**, 665-676.

CREEVY, C. D. AND FEENEY, M. J. (1954). Routine use of antibiotics in transurethral prostatic resection: a clinical investigation. *Journal of Urology*, **71**, 615-623.

GENSTER, H. G. AND MADSEN, P. O. (1970). Urinary tract infections following transurethral prostatectomy: with special reference to the use of antimicrobials. *Journal of Urology*, 104, 163-168.

KIDD, E. E., AND BURNSIDE, K. (1965). Bacteraemia, septicaemia and intravascular haemolysis during transurethral resection of the prostate gland. *British Journal of Urology*, **37**, 551-559.

LAST, P. M., HARBISON, P. A. and MARSH, J. A. (1966). Bacteraemia after urological instrumentation. *Lancet*, **1**, 74-76.

MEARES, E. M. and STAMEY, T. A. (1968). Bacteriologic localising patterns in bacterial prostatitis and urethritis. *Investigative Urology*, **5**, 492-518.

MILLER, A., GILLESPIE, W. A., LINTON, K. B., SLADE, N. and MITCHELL, J. P. (1958). Post-operative infection in urology. *Lancet*, **2**, 608-612.

MURNAGHAN, G. F., TYNAN, A. P., FARNSWORTH, R. H. and HARVEY, K. (1974). Chronic prostatitis—an Australian view. *British Journal of Urology*, **46**, 55-59.

PLORDE, J. J., KENNEDY, R. P., BOURNE, H. H., ANSELL, J. S. and PETERSDORF, R. G. (1965). Course and prognosis of prostatectomy with a note on the incidence of bacteremia and effectiveness of chemoprophylaxis. *New England Journal of Medicine*, 272, 269-277.

ROSEN, R. (1919). The bacterial content of the prostate and its relation to prostatic adenoma. *Journal of Infectious Diseases*, **24**, 63-75.

SCHMIDT, J. D. and PATTERSON, M. C. (1966). Needle biopsy study of chronic prostatitis. *Journal of Urology*, **96**, 519-533.

SCOTT, W. W. (1929). Blood stream infections in urology; report of 82 cases. *Journal of Urology*, **21**, 527-566.

SMART, C. J. and JENKINS, J. D. (1973). The role of transurethral prostatectomy in chronic prostatitis. *British Journal of Urology*, **45**, 654-662.

SYMES, J. M., HARDY, D. G., SUTHERNS, K. and BLANDY, J. P. (1972). Factors reducing the rate of infection after transurethral surgery. *British Journal of Urology*, **44**, 582-586.

WEAR, J. B. and HALEY, P. (1973). Transurethral prostatectomy without antibiotics. *Journal of Urology*, **110**, 436-440.

The Authors

Michael J. Morris, FRACS, Registrar, Department of Surgery.
David Golovsky, FRACS, Visiting Specialist, Department of Urology.
Michael D. G. Guinness, FRCPA, Director, Department of Microbiology.
P. O. Maher, FRCS, FRACS, Specialist-in-Charge, Department of Urology.

Requests for offprints to Dr Golovsky

British Journal of Urology (1976), **48**, 485-491 ©

Testosterone Metabolism in Benign Prostatic Hypertrophy: *in vivo* Studies of Gestonorone Caproate and Cyproterone Acetate

F. ORESTANO and J. E. ALTWEIN
Department of Urology, University of Mainz Medical School, Mainz, West Germany

There is good evidence indicating that growth and function of the human prostate are androgen-dependent (Moore, 1947; Gloyna, Siiteri and Wilson, 1970; Siiteri and Wilson, 1970). Among the circulating androgens from testicular and adrenal sources, testosterone is the main representative. It is able to enter the prostatic cell down a concentration gradient (Wilson, 1972). The involvement of other regulating factors such as prolactin has not been confirmed.

Inside the cell, testosterone is bound to a cytoplasmic ligand acting as a carrier receptor (Bruchovsky and Wilson, 1968; Mainwaring and Milroy, 1973). At the nuclear membrane of the prostatic cell (which contains nearly half the total enzymatic capacity of the entire cell) testosterone is reduced to 5α-dihydrotestosterone (DHT), which is the mediator of androgenic action (Moore and Wilson, 1972). DHT is bound to an intranuclear receptor and initiates the transcription of messenger RNA and the complex metabolic changes of androgen action (Wilson, 1972).

Attempts to alter the binding of androgens to cytoplasmic receptors within the human prostatic cell by means of oestrogens or antiandrogens were not successful (Steins *et al.*, 1974; Mobbs, Johnson and Connolly, 1975).

However, the long-acting gestagen gestonorone caproate (GC) was found to be a competitive inhibitor of the 5α-reduction of testosterone to its most potent intraprostatic androgen DHT (Orestano *et al.*, 1975). From the rat prostate, it has been concluded that cyproterone acetate (CA) inhibits the formation of the DHT-nuclear-receptor complex (Walsh and Korenman, 1971).

This mode of action has not been confirmed for man. Studying BPH tissue *in vitro*, Giorgi *et al.* (1973) noticed an increased androgen clearance in the presence of CA. Thus, an investigation of the mode of action exerted by the long-acting gestagen GC and the antiandrogen CA in patients with benign prostatic hypertrophy (BPH) not relying on *in vitro* techniques seemed warranted.

It is the objective of this paper to present the effect of GC and CA in different treatment regimes upon the testosterone and luteinising hormone (LH) level in plasma, the disappearance and turnover of H^3-testosterone injected intravenously, the uptake and the metabolism of H^3-testosterone in BPH-tissue.

Patients and Methods

18 patients aged 59 to 83 years (mean age 71·5 years) suffering from BPH were studied. Liver disease was excluded by measuring serum glutamic oxaloacetic transaminase, serum glutamic pyruvic transaminase, and serum alkaline phosphatase.

The following groups were arranged:

1. untreated patients serving as controls ($n = 4$),
2. patients receiving 200 mg GC (Depostat, Schering AG, Berlin, West Germany) intramuscularly *daily* for 5 days up to a total dose of 1,000 mg ($n = 6$),

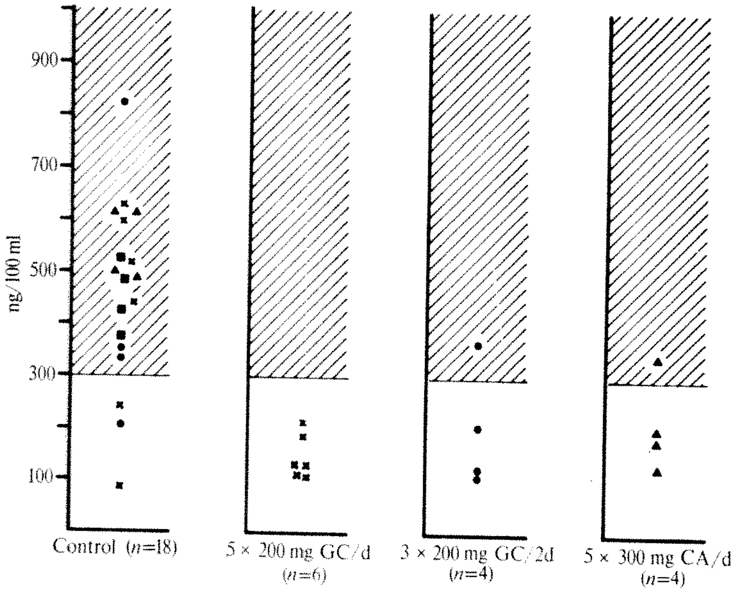


Fig. 1. Plasma testosterone level before and after treatment in groups 1 to 4., Control. **X**, 5 × 200 mg GC/d = daily injections of 200 mg gestonorone caproate for 5 days; ●, 3 × 200 mg GC/2d = administration of 200 mg gestonorone caproate on alternate days up to a total dose of 600 mg; ▲, 5 × 300 mg CA/d = daily injections of 300 mg cyproterone acetate for 5 days. Hatched areas = normal range.

3. patients being treated with 200 mg GC intramuscularly on *alternate days* up to a total dose of 600 mg ($n = 4$),
4. patients receiving 300 mg CA (Androcur, Schering AG, Berlin, West Germany) intramuscularly daily up to a total dose of 1,500 mg ($n = 4$).

At 7.30 a.m., blood samples were obtained for the determination of plasma testosterone and serum LH in single values. Plasma testosterone and serum LH were measured before the treatment and at the time of the experiment (7.40 a.m.), *i.e.*, 24 hours after discontinuation of the treatment in groups 2 to 4. 400 μCi H^3-testosterone in 10 ml of a 20% ethanol in isotonic saline solution was given in one arm vein. At 2, 5, 10, 15, 20 and 30 minutes after the injection, blood was drawn, and again at 90 minutes, when the prostatic tissue was resected transurethrally. The blood samples were collected in heparinised glass tubes. A portion of the BPH tissue was used for histological confirmation of the diagnosis.

7α-H^3-testosterone (Radiochemical Centre, Amersham, Bucks) had a specific activity of 5 Ci/mmol and was found to be more than 95% pure when examined by thin-layer chromatography on silica gel sheets (Merck, Darmstadt, West Germany) developed in the system hexane : methanol : water (5 : 4 : 1; v/v). The method used for extracting H^3-testosterone and its metabolites from plasma and tissue, for their identification and assessment of radioactivity has been described previously (Orestano *et al.*, 1975). The radioactivity was expressed as dpm (disintegrations per minute) which were computed from cpm (counts per minute) according to Stern and Eisenfeld (1971). Plasma testosterone and serum LH were determined by radioimmunoassay. The normal range for testosterone was between 300 and 1,200 ng per 100 ml and for LH less than 11 mIU/ml.

Results

15/18 patients with BPH had a plasma testosterone level within the normal range, whereas 3 patients displayed subnormal testosterone values before the onset of treatment (Fig. 1). The

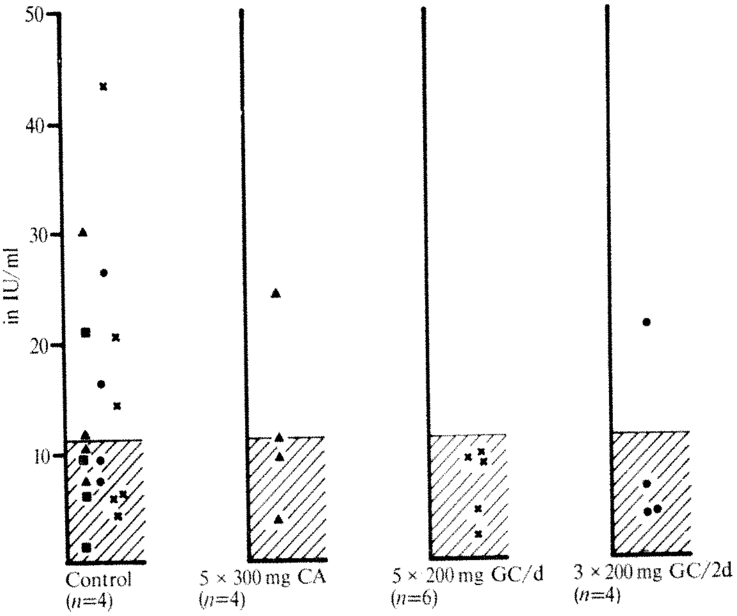


Fig. 2. Serum LH levels before and after treatment in groups 1 to 4. Hatched areas = normal range. mIU = milli International Units. See Figure 1 for symbols and abbreviations.

treatment regimens in groups 2-4 resulted in a decline of plasma testosterone below 300 ng/100 ml in 12 of the 14 patients in study.

10/18 patients had normal LH values (Fig. 2). In 5 of the 7 patients with initial LH elevation, the application of GC and CA resulted in a suppression of LH. The gradual disappearance of the level of radioactivity did not display significant differences between the 4 groups. The concentration of endogenous testosterone—< 300 ng/100 ml or between 300 and 600 ng/100 ml—was unrelated to the elimination of radioactivity.

H^3-testosterone accounted for the majority of radioactivity in plasma. Again, the different treatment regimens (groups 2-4) did not alter significantly the disappearance rate of H^3-testosterone in plasma (Fig. 3). There was no correlation between the initial level of endogenous testosterone—< 300 mg/100 ml or between 300 and 600 mg/100 ml—and the slope of the disappearance curve for H^3-testosterone in plasma (Fig. 3).

Among the H^3-testosterone metabolites, the 5α-reduction products DHT and 5α-androstane 3α-17β-diol ranged 1st and 2nd. The timecourse of DHT and 5α-androstane 3α-17β-diol revealed a peak concentration at 15 minutes after the injection of H^3-testosterone (appearance rate) declining towards baseline at 90 minutes (disappearance rate). The appearance and disappearance rates were found in the same range for groups 2 to 4, however, the difference from group 1 (control) was not statistically significant. The preinjection level of endogenous testosterone was not related to the amount of H^3-testosterone metabolites found. The uptake of radioactivity into the prostatic tissue was significantly ($P < 0{\cdot}05$) repressed in group 2, but elevated in group 3 ($P < 0{\cdot}05$) (Fig. 4).

The lowest concentration of H^3-testosterone in prostatic tissue was encountered in group 2, being significantly different ($P < 0{\cdot}05$) from group 1 and 3 (Fig. 4).

The concentration of the 5α-reduction products, H^3-DHT and H^3-5α-androstane 3α-17β-diol, in BPH reflects the reduction capacity of the prostate in regard to T (Frederiksen and Wilson, 1971). The concentration of these 5α-reduction products in group 3 and 4 exceeded group 1 at $P < 0{\cdot}01$, whereas daily injections of 200 mg GC (group 2) resulted in a significant inhibition

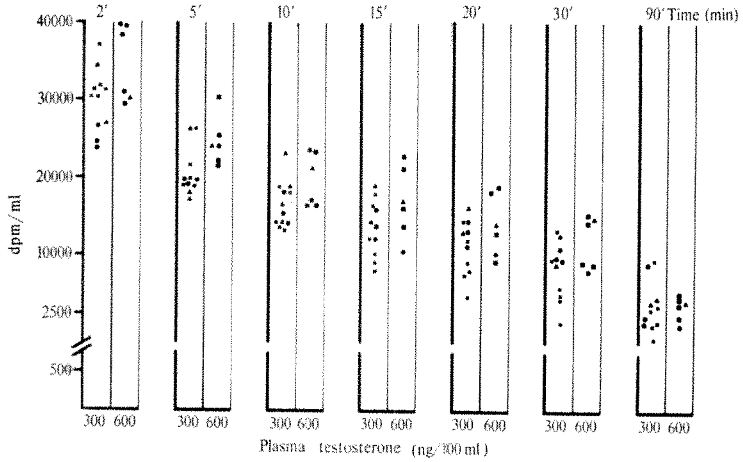


Fig. 3. H^3-testosterone values of all patients as a function of the time of blood withdrawal. Each panel is divided according to the endogenous testosterone level before the onset of the experiment. dpm = disintegrations per minute. Symbols as in Figure 1.

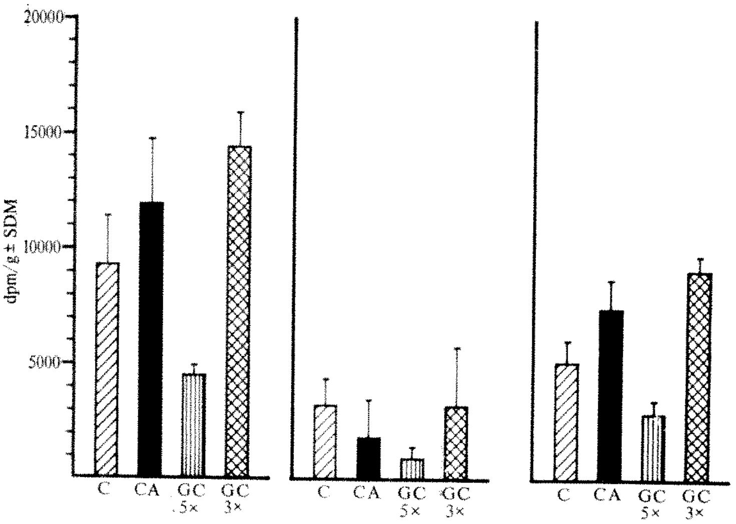


Fig. 4. Total radioactivity (left panel), H^3-testosterone (middle panel), and H^3-5α-reduction metabolites (right panel) according to mode of treatment. SDM = standard deviation of the mean. C, control. For abbreviations see Figure 1.

($P < 0{\cdot}01$) of the 5α-reduction of H^3-testosterone in BPH. However, the percent-distribution of H^3-testosterone and its 5α-reduction products were equal in each group. Neither a positive nor a negative correlation between the pre-injection level of endogenous testosterone was demonstrable (Fig. 5).

Discussion

All the male patients included in this investigation had normal testosterone and LH levels at the onset of the study as measured according to Vermeulen, Rubens and Verdonck (1972). They determined a normal plasma testosterone in healthy men aged 60 to 70 years of 462 ± 70 ng/100

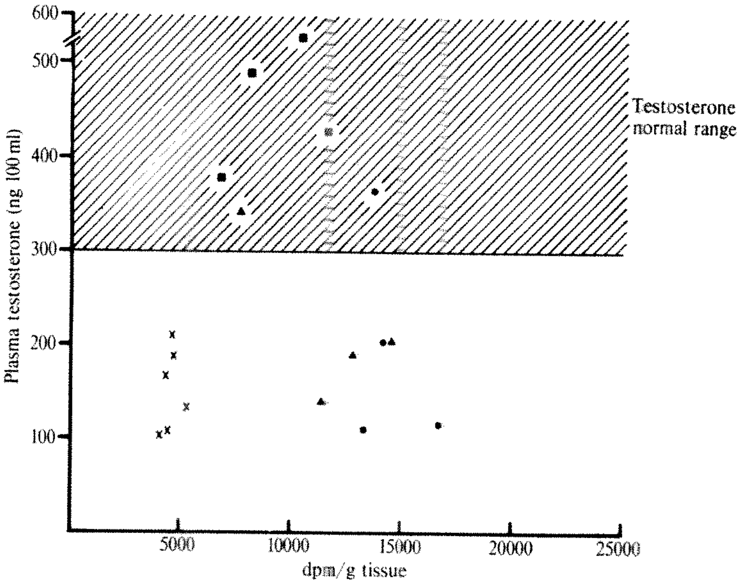


Fig. 5. Correlation between the content of total radioactivity in BPH tissue and the endogenous testosterone level in plasma before the onset of the experiment. For symbols see Figure 1.

ml (range 120-870) and in men between 70 and 80 years of 373 ± 46 ng/100 ml (range 38-850). In regard to LH, a mean level of 22·5 mIU/ml (range 15·8-31·7) was considered normal for men older than 65 years (Vermeulen, 1975).

The long-acting gestagen GC in both dosages tested as well as CA resulted in decrease of endogenous T in plasma and LH in serum. This is consistent with the findings of Clark, Calandra and Bird (1972), Gordon *et al.* (1972) and Murray *et al.* (1973).

Clark *et al.* (1972) observed in young men that a 10-day treatment with medroxy-progesterone acetate resulted in inconclusive changes of the metabolic clearance rate. In the present study also, no effect of the 3 treatment regimens in regard to the disappearance of total radioactivity and H^3-testosterone from plasma was found. This also applies to the peripheral metabolism of H^3-testosterone as indicated by the amount of 5α-reduction products present in plasma.

Orestano *et al.* (1975) have shown that H^3-testosterone enters the human prostate selectively, *i.e.*, as compared to muscle or urinary bladder. GC treatment (1,000 mg over 5 days) resulted in a striking impediment of uptake radioactivity into BPH-tissue. This gestagenic effect is presumably related to a lowered blood production rate of endogenous testosterone; accordingly, to an increased binding with a decreased metabolic clearance rate (Gordon *et al.*, 1972); and finally, to a blockade of the cytoplasmic receptor for testosterone. The latter effect, however, cannot be complete as demonstrated by the still on-going formation of 5α-reduction products of H^3-testosterone within the prostatic cells.

A reverse behaviour was found for the prostate in relation to CA and GC (administered on alternate days). CA is effective in competing for the nuclear receptor of the target organ as evidenced by animal studies (Walsh and Korenman, 1971), but not interfering with the H^3-testosterone uptake into the cytoplasm, the first compartment of entry into the prostate. Therefore, Giorgi *et al.* (1973) investigating BPH tissue *in vitro*, were unable to find an inhibition of the 5α-reduction of the testosterone. This is in keeping with the unchanged 5α-reduction of H^3-testosterone *in vivo*.

GC is used in dosages ranging from 200 to 800 mg weekly for the relief of minor BPH-related symptoms. Thus GC was studied in 2 different doses (groups 2 and 3). The increased radioactivity and H^3-testosterone content in the prostate (group 3) is apparently not related to a rebound-effect with a subsequent LH-surge, but it is proposed that GC is primarily incorporated into the prostate along a concentration gradient liberating a sufficient number of target organ "ligands". If the GC-application is discontinued for 48 hours as in group 3, the intraprostatic GC is further processed or released, and thus the influxing testosterone might well be bound to a larger number of receptors than in group 2.

In essence, this study demonstrates that the long-acting gestagen gestonorone caproate and the anti-androgen cyproterone acetate given to patients with BPH are effective in suppressing the plasma testosterone and serum LH. At the target organ level, only GC administered daily was able to inhibit the uptake and metabolism of tritiated testosterone, whereas GC given on alternate days or CA did not show this effect.

Summary

18 patients with obstructive benign prostatic hypertrophy were studied.

A 5-day treatment with gestonorone caproate (200 mg daily and 200 mg on alternate days) and cyproterone acetate (300 mg daily) suppressed the plasma LH and serum LH levels. Subsequently, H^3-testosterone was injected intravenously and its elimination from plasma and uptake and metabolism in the BPH tissue studied. The elimination of total radioactivity and H^3-testosterone from plasma was not altered after the 3 treatment regimens as compared to the control group. The uptake of total radioactivity into BPH tissue and its intraprostatic metabolism particularly to dihydrotestosterone was significantly suppressed in the patients with daily injections of gestonorone. Cyproterone acetate and gestonorone caproate on alternate days did not cause this effect.

Supported by the Helmut Horten Foundation.

References

Bruchovsky, N. and Wilson, J. D. (1968). Intranuclear binding of testosterone and 5α-androstan-17β-01-3-one by rat prostate. *Journal of Biological Chemistry*, **243**, 5953-5960.

Clark, A. F., Calandra, R. S. and Bird, C. E. (1972). Kinetics of (^3H)-testosterone metabolism in normal young men: effects of medroxyprogesterone acetate (provera) administration. *Journal of Steroid Biochemistry*, **3**, 837-842.

Frederiksen, D. W. and Wilson, J. D. (1971). Partial characterization of the nuclear reduced nicotinamide adenine dinucleotide phosphate: Δ^4-ketosteroid 5α-oxidoreductase of rat prostate. *Journal of Biological Chemistry*, **246**, 2584-2593.

Giorgi, E. P., Shirley, I. M., Grant, J. K. and Stewart, J. C. (1973). Androgen dynamics *in vitro* in the human prostate gland: effect of cyproterone and cyproterone acetate. *Biochemical Journal*, **132**, 465-474.

Gloyna, R. E., Siiteri, P. K. and Wilson, J. D. (1970). Dihydrotestorone in prostatic hypertrophy. II. The formation and content of dihydrotestosterone in the hypertrophic canine prostate and the effect of dihydrotestosterone on prostate growth in the dog. *Journal of Clinical Investigation*, **49**, 1746-1753.

Gordon, G. G., Southren, A. L., Calanog, A., Olivo, J. and Rafii, F. (1972). The effect of medroxyprogesterone acetate on androgen metabolism in the polycystic ovary syndrome. *Journal of Clinical Endocrinology and Metabolism*, **35**, 444-447.

Mainwaring, W. I. P. and Milroy, E. J. G. (1973). Characterization of the specific androgen receptors in the human prostate gland. *Journal of Endocrinology*, **57**, 371-384.

Mobbs, B. G., Johnson, I. E. and Connolly, J. G. (1975). *In vitro* assay of androgen binding by human prostate. *Journal of Steroid Biochemistry*, **6**, 453-458

Moore, R. A. (1947). Benign hypertrophy and carcinoma of the prostate. In *Endocrinology of Neoplastic Diseases*, ed. by G. H. Twombly and G. T.Pack. New York: Oxford University Press, pp. 194-212.

Moore, R. J. and Wilson, J. D. (1972). Localisation of reduced nicotinamide adenine dinucleotide phosphate Δ^4-3-ketosteroid 5α-oxido reductase in the nuclear membrane of the rat ventral prostate. *Journal of Biological Chemistry*, **247**, 958-967.

Murray, M. A. F., Anderson, D. C., Bancroft, J. H. J., Tennant, T. G. and Carr, P. J. (1973). Sex-hormone-binding globulin, luteinizing hormone and testosterone in man: effects of oestrogen and cyproterone acetate. *Journal of Endocrinology*, **59**, xxi-xxii.

ORESTANO, F., ALTWEIN, J. E., KNAPSTEIN, P. and BANDHAUER, K. (1975). Mode of action of progesterone, gestonorone capronate (depostat) and cyproterone acetate (androcur) on the metabolism of testosterone in human prostatic adenoma: *in vitro* and *in vivo* investigations. *Journal of Steroid Biochemistry*, **6**, 845-851.

SIITERI, P. K. and WILSON, J. D. (1970). Dihydrotestosterone in prostatic hypertrophy. I. The formation and content of dihydrotestosterone in the hypertrophic prostate of man. *Journal of Clinical Investigation*, **49**, 1737-1745.

STEINS, P., KREIG, M., HOLLMANN, H. J. and VOIGT, K. D. (1974). *In vitro* studies of testosterone and 5α-dihydrotestosterone binding in benign prostatic hypertrophy. *Acta Endocrinologica*, **75**, 773-784.

STERN, J. M. EISENFELD, A. J. (1971). Distribution and metabolism of ^{3}H-testosterone in castrated male rats; effects of cyproterone, progesterone and unlabeled testosterone. *Endocrinology*, **88**, 1117-1125.

VERMEULEN, A., RUBENS, R. and VERDONCK, L. (1972). Testosterone secretion and metabolism in male senescence. *Journal of Clinical Endocrinology and Metabolism*, **34**, 730-735.

VERMEULEN, A. (1975). Leydig-Zell-Funktion im Alter. *Aktuelle Urologie*, **6**, 247-251.

WALSH, P. C. and KORENMAN, S. G. (1971). Mechanism of androgenic action: effect of specific intracellular inhibitors. *Journal of Urology*, **105**, 850-857.

WILSON, J. D. (1972). Recent studies on the mechanism of action of testosterone. *New England Journal of Medicine*, **287**, 1284-1291.

The Authors

Fausto Orestano, MD, Professor of Urology, Chief, Casa di Cure Orestano, Palermo.

Jens E. Altwein, MD, Professor of Urology, Oberarzt, Department of Urology, University of Mainz Medical School.

Reprint requests to: J. E. Altwein, MD, Department of Urology, University of Mainz Med. School, D-6500 Mainz, West Germany.

British Journal of Urology (1976), **48**, 492 ©

Short Case Report

Obstructing Prostatic Urethral Calculi

Giant prostatic urethral calculi are rare, but may occasionally cause urinary infection and obstruction. Although they may have begun as true prostatic calculi, these giant stones generally destroy much of the prostate gland and may require a different therapeutic approach.

Case Report

An 82-year-old white male was admitted for evaluation of recurrent urinary tract infection with obstructive and irritative urinary symptoms.

Physical examination revealed an enlarged, stony hard prostate. Urine culture showed greater than 100,000 organisms per cubic centimetre of *Proteus mirabilis*. Excretory urogram demonstrated two large calculi on the plain film (Fig.). The lower calculus was in the prostatic urethra, while the upper calculus was situated in the bladder. The bladder exhibited trabeculation and several diverticula. The upper collecting systems were normal. Urethroscopy revealed a normal anterior urethra and complete obstruction of the prostatic urethra by an enormous calculus. A suprapubic approach was used to remove the vesical stone. Vesical neck incision was needed to extract the giant stone which was located entirely in the prostatic urethra. Bimanual examination revealed only a thin rim of remaining prostatic tissue. The vesical calculus weighed 27 grams and the prostatic calculus 40 grams. X-ray diffraction crystallography of the vesical calculus revealed 90% magnesium ammonium phosphate, whereas the prostatic calculus was composed of 85% carbonate apatite (tri-calcium phosphate) and 15% magnesium ammonium phosphate. The patient's postoperative course was uneventful.

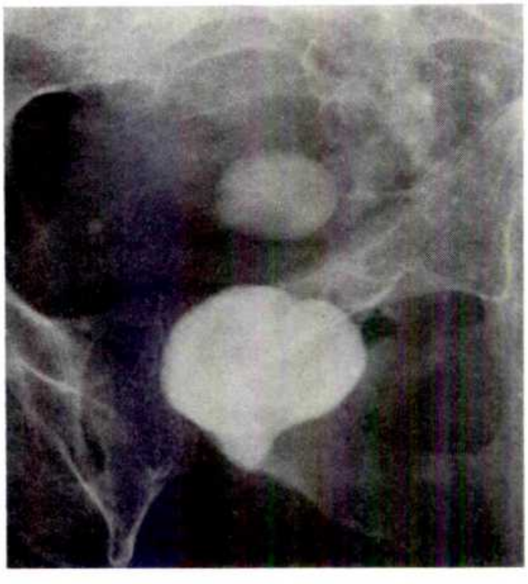


Fig.

Comment

The management of prostatic calculi depends on their size, location, and the presence of urinary tract infection. True prostatic calculi are usually small and located in the periphery of hyperplastic glands, residing between the adenoma and the compressed prostatic tissue. In the presence of obstructive symptoms with persistent infection, enucleation or transurethral resection of the prostate with removal of the calculi is necessary to remove the obstruction and to eliminate a nidus for infection. When, however, a giant prostatic urethral calculus is the cause of both obstruction and urinary infection, enlargement of the stone and pressure atrophy of the prostate gland may have simplified its management. In this situation, as in the present case, suprapubic removal of the stone with vesical neck revision will probably suffice to relieve obstruction and infection. No formal attempt at removing prostate tissue is necessary, since an "autoprostatectomy" has already occurred, probably secondary to pressure and infection.

ROBERT K. VINSON and STEPHEN A. KOFF
Section of Urology, Department of Surgery, University of Michigan Medical Center, Ann Arbor, Michigan.

References

FOX, M. (1963). The natural history and significance of stone formation in the prostate gland. *Journal of Urology*, **89**, 716.

SUTOR, D. J. and WOOLEY, S. E. (1974). The crystalline composition of prostatic calculi. *British Journal of Urology*, **46**, 533.

British Journal of Urology (1976), **48**, 493–497 ©

Detrusor and Urethral Dysfunction in Prostatic Hypertrophy

JENS T. ANDERSEN and WILLIAM E. BRADLEY

Department of Neurology, University of Minnesota, Minneapolis 55455, Minnesota

The traditional methods of evaluation of patients with symptoms and signs of prostatic hyperplasia have been based upon clinical, radiographic and endoscopic investigations for evidence of anatomic obstruction of the lower urinary tract. In recent studies, uroflowmetry (Shoukry *et al.*, 1975), combined urodynamic (Claridge and Shuttleworth, 1964; Turner-Warwick and Whiteside, 1969) and uro-radiologic (Shopfner, 1965) studies have further delineated the hydrodynamics of obstructed micturition. However, 2 recent modes of investigation have impacted upon the conventional method of patient assessment and conceptualisation. These methods combine assessment of detrusor and urethral function utilising detrusor reflex activation procedures as well as urethral function tests. From these methods patients have been determined to have detrusor reflex instability as well as urethral changes. Transurethral resection of the prostate (TURP) has been shown to increase flow rate not by depressing urethral tension but shortening urethral length. Further, TURP had no effect on maximal intramural urethral pressure.

Method

Detrusor reflex function was assessed by means of gas cystometry (Bradley *et al.*, 1975) and assessment of detrusor reflex instability utilising the effects of posture. Carbon dioxide was infused into the bladder with an indwelling catheter at rates up to 300 cc/min. Detrusor reflex activation procedures employed included testing in supine and upright positions, subcutaneous administration of bethanechol (Lapides *et al.*, 1962) and urethral and rectal distension.

Urethral function was investigated by combined electromyographic and gas urethral pressure profilometry (Andersen and Bradley, 1976). Intra-urethral pressure was measured during urethral traverse of a recording catheter from the bladder neck to the membranous urethra by a constant velocity catheter puller. Concurrent recording of striated muscle activity was recorded at the site of measurement of the urethral pressure profile.

Urinary flow rates were obtained using a load-cell flowmeter based on the principle of Von Garrelts (Von Garrelts and Strandell, 1972). Accuracy of maximum flow was $\pm 1\%$.

Results

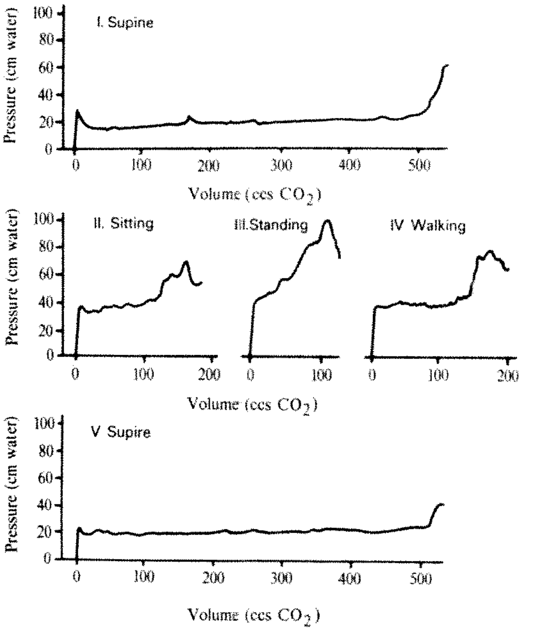
9 males with prostatic enlargement were studied before and 3 months after transurethral resection of the prostate. The histologic examination of the resected tissue revealed benign hyperplasia in 5 patients and adenocarcinoma in the remaining 4 patients. None of the patients presented evidence of focal neurological disease. The patients had a mean age of 74·2 years (range: 58–83 years). The symptoms of prostatic hypertrophy had a mean duration of 3·3 years (range: 1–10

Table I

Results of Gas Cystometry including Detrusor Reflex Activating Procedures in 9 Patients before and 3 months after Transurethral Resection of the Prostate

Cystometric Results	Preoperative (No. of patients)	Postoperative (No. of patients)
Normal cystometrogram	2	1
Detrusor hyperreflexia	4	2
Postural detrusor hyperreflexia	1	3
Detrusor areflexia	1	2
Increased tonus limb	1*	0

* Died before the postoperative examination.



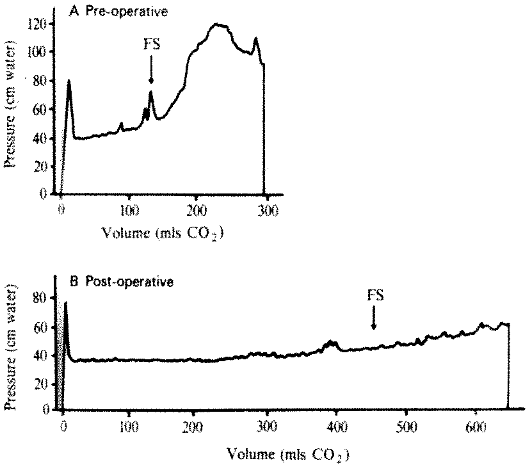


Fig. 1 (left). Gas cystometrograms showing postural detrusor hyperreflexia.

Fig. 2 (right). Cystometric findings in a 77-year-old man (*a*) before; (*b*) 3 months after TURP (adenocarcinoma).

years). Urine cultures taken preoperatively and 3 months after TURP showed significant bacteriuria in 4 patients preoperatively and in 1 patient postoperatively.

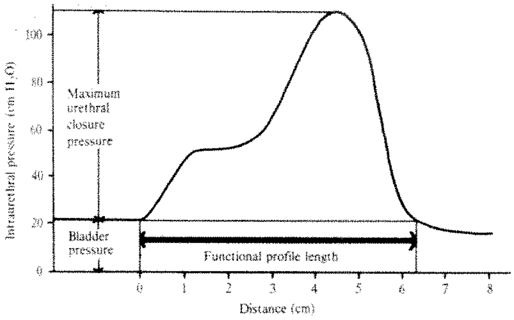
The cystometric results are summarised in Table I. A *normal cystometrogram* was one with normal sensation of fullness and the presence of a detrusor reflex which could be voluntarily suppressed on command. *Detrusor hyperreflexia* was defined as a detrusor reflex evoked at low bladder distension which the patient could not voluntarily suppress. *Postural hyperreflexia* evoked by changing the test subject's position from supine to upright (Fig. 1) was observed in 1 patient.

Detrusor areflexia was defined as a cystometrogram showing absence of the reflex during bladder filling and detrusor reflex activation procedures. 5 patients demonstrated detrusor hyperreflexia preoperatively and 1 demonstrated detrusor areflexia. 1 of the patients with detrusor hyperreflexia preoperatively demonstrated areflexia postoperatively (Fig. 2) and 2 patients, 1 with hyperreflexia and 1 with a normal cystometrogram preoperatively demonstrated postural hyperreflexia postoperatively.

Urine cultures taken during the pre- and postoperative examination showed no correlation between presence of detrusor hyperreflexia and significant bacteriuria.

Combined EMG and Gas Urethral Pressure Profiles

The urethral pressure profiles were analysed according to the recommendations of the International Continence Society (Bates *et al.*, 1976) (Fig. 3). The mean values and ranges of *functional profile length* and *maximum urethral closure pressure* are tabulated in Table II. A significant reduction was found in the functional profile length after TURP, whereas no change was found in the maximum urethral closure pressure. The maximum urethral closure pressure is located to the membranous urethra (Andersen *et al.*, 1976) and TURP was not expected to affect this parameter (Fig. 4).


Intraurethral pressure (cm H$_2$O)
100
80
60
40
20
0
Maximum urethral closure pressure
Bladder pressure
Functional profile length
0 1 2 3 4 5 6 7 8
Distance (cm)

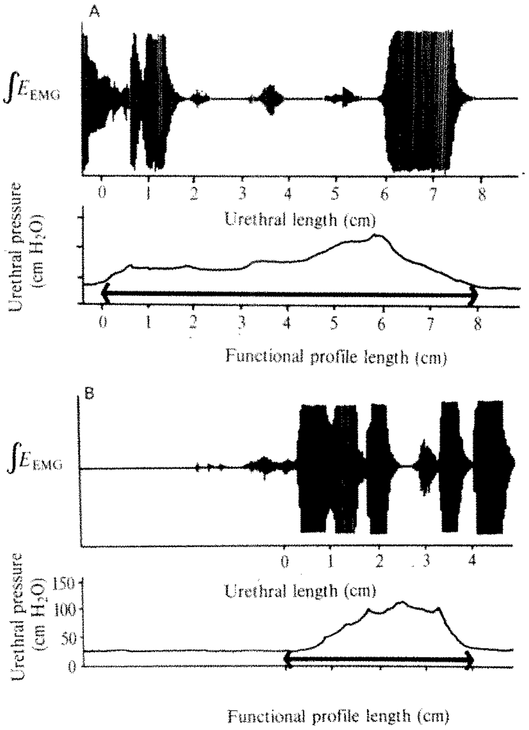


Fig. 3 (left). Schematic illustration of the delineation of urethral pressure profile parameters.

Fig. 4 (right). Combined electromyographic and gas urethral pressure profiles from an 83-year-old man (*a*) before; (*b*) after TURP (benign hyperplasia). Note the reduction in functional profile length.

Table II

Urethral Pressure Profile Parameters before and after TURP in 9 Consecutive Patients

	Preoperative ($n=9$)		Postoperative ($n=8$)	
	Functional profile length (cm)	Maximum urethral closure pressure (cm H_2O)	Functional profile length (cm)	Maximum urethral closure pressure (cm H_2O)
Mean value	6·3	85·0	4·3	84·4
Range	3·5–8	58–116	2·5–6	4–160

Table III

Results of Uroflowmetry before and 3 months after TURP

	Maximum flow-rate (ml/sec)	Average flow-rate (ml/sec)	Voided volume (ml)	Voiding time (sec)	Residual volume (ml)
Preoperative ($n=5$) Mean (Range)	8·2 (4–12)	4·2 (1·6–6·5)	166 (40–325)	38 (25–50)	18·6 (1–70)
Postoperative ($n=8$) Mean (Range)	13·9 (4–22)	6·1 (2–11)	217 (80–300)	43 (20–114)	38 (1–180)

Uroflowmetry

5 patients were able to micturate during the preoperative examination whereas all 8 patients had a free micturition 3 months postoperatively. The parameters obtained are summarised in Table III. The mean maximum flow rate was significantly increased after the resections and the voided volumes increased. The increase in mean residual volume postoperatively is due to the patient who developed detrusor areflexia with unbalanced bladder function after the TURP.

Discussion

Patients with prostatic hypertrophy may demonstrate one of several patterns of symptomatology. These include: (1) *irritative*, with frequency and urgency, and (2) *obstructive*. It is generally agreed that surgical therapy is addressed to the latter group.

In this series of patients with obstructive manifestations certain surprising aspects of detrusor and urethral function were observed as the result of the application of gas cystometry and combined gas and electromyographic urethral profiles.

A high incidence of detrusor hyperreflexia was observed in a manner similar to that reported in a prior study utilising water cystometry (Andersen, 1976). Further, the use of detrusor reflex activation procedures in this study whose application was facilitated by gas cystometry further defined this abnormality. Detrusor hyperreflexia occurring in patients with bladder outlet obstruction but without obvious neurological disease can be thought of as due to an increased input of detrusor reflex triggering stimuli from the heavily sensory innervated posterior urethra.

Sensory stimuli in this area would be caused by anatomical distortion and compression of nerve endings due to glandular enlargement in a manner analogous to an entrapment neuropathy.

The change in detrusor reflex function discovered in some of the patients after surgery to the prostate was explained by the *decompression* or *injury* of nerve endings in the prostate urethra.

The results of combined EMG and gas urethral pressure profilometry did not demonstrate increase in urethral closure pressure compared to healthy volunteers but consistently demonstrated increase in urethral length. The result of TURP was to decrease urethral length without significantly altering urethral closure pressure. The resultant change in functional urethral length resulted in increased efficiency of voiding and urinary flow.

In conclusion, patients with obstructive uropathy of the lower urinary tract secondary to prostatic hypertrophy demonstrate increase in urethral length and frequently detrusor hyperreflexia. The result of TURP is to decrease urethral length and hence increase the efficiency of voiding.

Summary

Assessment of bladder and urethral function in 9 patients with prostatic hypertrophy before and after transurethral resection of the prostate was performed utilising gas cystometry, detrusor reflex activating procedures, combined electromyographic and gas urethral pressure profilometry and uroflowmetry.

A high incidence of detrusor hyperreflexia was found preoperatively indicating neurogenic dysfunction of the bladder. Removal of the obstructive tissue implied a change in detrusor reflex function in a part of the patients confirming the findings from a larger series studied with water-cystometry. Decompression or injury of sensory nerve endings in the prostatic urethra thus seem to determine detrusor function after surgery to the prostate.

The impact of the resection upon urethral function was an increase in maximum urinary flow due to a significant shortening of the functional urethral length. No change in maximum urethral intramural pressure could be demonstrated.

References

ANDERSEN, J. T. (1976). Detrusor hyperreflexia in benign infravesical obstruction. *Journal of Urology*, **115**, 532-534.

ANDERSEN, J. T. and BRADLEY, W. E. (1976). The urethral closure pressure profile. *British Journal of Urology*, **48**, 341-345.

ANDERSEN, J. T., BRADLEY, W. E. and TIMM, G. W. (1976). The urethral electromyographic and gas pressure profile. *Scandinavian Journal of Urology and Nephrology* (in press).

BATES, P., BRADLEY, W. E., GLEN, E., MELCHIOR, H., ROWAN, D., STERLING, A. and HALD, T. (1976). Function of lower urinary tract: standardization of terminology, incontinence, cystometry, urethral pressure profile and measuring units. *Urologe A*, **15**, 93-96.

BRADLEY, W. E., TIMM, G. W. and SCOTT, F. B. (1975). Cystometry I: Introduction. *Urology*, **5**, 424-427.

CLARIDGE, M. and SHUTTLEWORTH, K. E. D. (1964). The dynamics of obstructed micturition. *Investigative Urology*, **2**, 188-199.

LAPIDES, J., FRIEND, C. R., AJEMIAN, E. P. and REUS, W. S. (1962). Denervation supersensitivity as a test for neurogenic bladder. *Surgery, Gynecology and Obstetrics*, **114**, 241-244.

SHOPFNER, C. E. (1965). Cystourethrography: an evaluation of method. *American Journal of Roentgenology*, **95**, 468-474.

SHOUKRY, I., SUSSET, J. G., ELHILALI, M. M. and DUTARTRE, D. (1975). Role of uroflowmetry in the assessment of lower urinary tract obstruction in adult males. *British Journal of Urology*, **47**, 559-566.

TURNER-WARWICK, R. T. and WHITESIDE, C. G. (1970). Investigation and management of bladder neck dysfunction. In *Modern Trends in Urology 3*. Ed. Sir E. Riches. London: Butterworth, pp. 295-311.

VON GARRELTS, B. and STRANDELL, P. (1972). Continuous recording of urinary flow rate. *Scandinavian Journal of Urology and Nephrology*, **6**, 224-227.

The Authors

Jens T. Andersen, MD, Assistant Professor.
William E. Bradley, MD, Professor.

British Journal of Urology (1976), **48**, 498 ©

Short Case Report

Testicular Metastasis from Prostatic Carcinoma

Secondary growths in the testis are rare (Pienkos and Jablokow, 1972). The commonest primary sites are the bronchus and prostate and the patients are normally in their sixties (Price and Mostofi, 1957). The growths, which may be multiple or solitary, are mostly asymptomatic and tend to be discovered at postmortem examination (Hanash *et al.*, 1969). The case reported is such a chance finding in a patient with adenocarcinoma of the prostate whose hormonal status had been modified by stilboestrol therapy.

Case Report

A 64-year-old mechanic presented in 1972 with haematuria and a 6-month history of persistent discomfort in the right loin. All relevant tests were normal, with the exception of an elevated blood urea (69 mg %). He underwent cystoscopy and transurethral resection of prostate, making an uneventful recovery. The histology was that of a well-differentiated adenocarcinoma and he was discharged taking stilboestrol 5 mg t.i.d.

Apart from several episodes of urinary tract infection, he remained well and the prostate stayed small and soft. In September 1973 he stopped taking stilboestrol because of his impotence. His condition was satisfactory over the next 12 months but he did not regain his sexual potency. At this time (September 1974) a skeletal survey showed evidence of asymptomatic pelvic and spinal metastases.

He was readmitted in February 1975, with renewed haematuria, pain in the right ear and diplopia. On examination, he had multiple right-sided cranial nerve palsies (Sensory V, VI, VII, XII). Straight X-rays of the skull disclosed an area of bony resorption in the right petrous temporal bone.

Accordingly, bilateral subcapsular orchidectomy was performed and local irradiation was given to the skull lesion. Histology of the testes showed marked maturation arrest, and in one an island of well-differentiated adenocarcinoma (Fig.) consistent with an origin in the prostate was found.

Comment

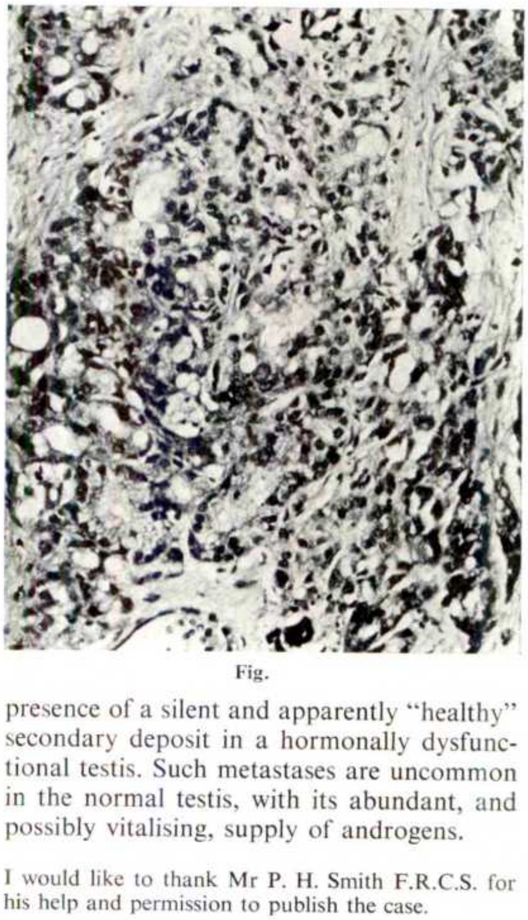


Fig.

This case demonstrates a rare complication of a common disorder. Of interest is the presence of a silent and apparently "healthy" secondary deposit in a hormonally dysfunctional testis. Such metastases are uncommon in the normal testis, with its abundant, and possibly vitalising, supply of androgens.

I would like to thank Mr P. H. Smith F.R.C.S. for his help and permission to publish the case.

N. P. Silverton
Department of Urology, Leeds (St James's) University Hospital, Leeds.

References

Hanash, K. A., Carney, J. A. and Kelalis, P. P. (1969). Metastatic tumours to testicles: Routes of metastases. *Journal of Urology*, **102**, 465-468.

Pienkos, E. J. and Jablokow, V. R. (1972). Secondary testicular tumours. *Cancer*, **30**, 481-485.

Price, E. B. and Mostofi, E. K. (1959). Secondary carcinoma of the testis. *Cancer*, **10**, 592-595.

British Journal of Urology (1976), 48, 499–503 ©

Artificial Insemination (A.I.H.) for Sperm Antibodies and Oligozoospermia

M. MCD. USHERWOOD, A. HALIM and P. R. EVANS
Department of Urology, The London Hospital, London E1 1BB

Although artificial insemination with husband's semen (A.I.H.) has a long history, in recent years there has been a tendency to regard it as valueless when the husband's semen is of poor quality. In a variety of conditions, *e.g.* retrograde ejaculation, low sperm density, low sperm motility, sperm antibodies and cervical "hostility", 19 pregnancies were achieved in 2 years. This has led us to believe that the method is valuable, given that there are several imperfections.

Patients

The patients were of a varied background and occupation. The ages of the women varied from 22 to 39 years, whilst the age range of the men was 22 to 59 years. The couples had been infertile for from 2 to 14 years.

Investigations

Couples were assessed in an infertility clinic jointly by gynaecologists and urologists. The following investigations were performed on the women.

Ovulation was assessed by endometrial biopsy and basal body temperature records. Tubal patency was at first checked by hystero-salpingography and later in the series by laparoscopy and dye hydrotubation. Cervical "hostility" was studied by 2 or more post-coital tests. Plasma sperm agglutinating antibodies were measured by Kibrick's method (Kibrick, Belding and Merrill, 1952) as modified by Halim and Antoniou (1973*a*): a titre of more than 1 : 32 was regarded as significant (Rumke, 1975).

The men were investigated according to the scheme described by Halim *et al.* (1973*b*).

Treatment

Where appropriate ovulation was induced in women with clomiphene citrate. Men with low sperm densities were given clomiphene citrate 50 mg daily and/or fluoxymesterone 5 mg daily (Halim *et al.*, 1973*b*). The A.I.H. therapy was started at a time when a good response to clomiphene citrate or fluoxymesterone had been noted, usually after an 8-week course of treatment. At first A.I.H. was offered, (*a*) when the sperm density was more than 3×10^6/ml; a count later raised to more than 10×10^6/ml; (*b*) when the motility was more than 30%; (*c*) if antibodies were demonstrated in either partner and (*d*) if cervical "hostility" had been demonstrated. Those with small volumes of semen were not necessarily considered as needing A.I.H. therapy. Volume of sperms inseminated was always 1 ml.

Method of A.I.H.

Our patients came from a wide area, sometimes travelling as far as 280 miles and it was not feasible to attempt A.I.H. more than once during a menstrual cycle. Therefore, we attempted to select the day nearest to ovulation. The couple were asked to abstain from intercourse for a week before the husband produced a fresh specimen of semen on the day of insemination. On arrival at the clinic, each semen sample was assessed for count and motility.

An equal volume of phosphate buffer solution was added with aseptic precautions and the whole specimen was centrifuged at 500 rpm for 20 min. The sperm deposit was resuspended in phosphate buffer and centrifuged for a second time for 20 min at 500 rpm and finally resuspended in 1 ml of phosphate buffer solution at room temperature. In those men with retrograde ejaculation, sperms were recovered from urine voided immediately after ejaculation, the urine having previously been alkalinised by ingestion of 3 days of sodium bicarbonate. The sperms were prepared in the same way as described above. If there was autoagglutination or a strongly positive male Kibrick test the washing and suspension of the sample was performed 3 times. When either partner had a positive Kibrick test then he or she was given prednisolone 5 mg t.d.s. for the first 2 weeks of the wife's cycle.

The woman sat in a cystoscopic chair for the insemination. The vulva, vagina and cervix were thoroughly cleansed with 1% sodium bicarbonate solution. The semen was injected slowly with a disposable 1 ml insulin syringe and No. 12 Intracath cannula, taking care to place the tip of the cannula no more than 2 cm inside the cervical os and to avoid excessive manipulation of the cervix. After insemination the patient lay down with her buttocks supported by a pillow for about 15 min. 6 inseminations were performed in each case before the situation was reviewed.

Indications for A.I.H.

The indications for A.I.H. therapy of the 74 couples treated in 2 complete years are shown in Table I.

The effects of treatment given to 41 partners prior to A.I.H. in terms of improving the sperm density or motility are shown in Table II. The resulting sperm counts in all of the men prior to A.I.H. are given in Table III.

Results

The details of the couples in whom pregnancies occurred are given in Table IV.

Table V gives an indication of the success rate in terms of sperm density and motility at the start of A.I.H. therapy.

The number of inseminations required before the 19 pregnancies were achieved varied greatly. 13 pregnancies resulted during the first 6 inseminations, with a further 5 during the second 6

Table I

The Indications for A.I.H.

Indication	Nos.	
Density of less than 20 × 10⁶/ml without treatment	37	3 with associated indications
Motility of less than 30% without treatment	19	7 with associated indications
Autoagglutination of sperms	2	
Retrograde ejaculation	3	
Positive Kibrick greater than 1 in 64 in either partner	11	7 with associated indications
Positive Kibrick less than 1 in 64 in either partner	3	
Cervical "hostility"	13	2 with associated indications
Ovulation irregularity	8	6 with associated indications
Total	96	25

Table II

Results of Treatment to 41 Patients with Clomiphene Citrate and/or Fluoxymesterone

	Before treatment	After treatment
Sperm density		
Less than 5 × 10⁶/ml	15	0
5-10 × 10⁶/ml	10	7
10-50 × 10⁶/ml	2	20
Sperm motility		
Less than 30%	17	7
More than 30%	0	10

3 patients were treated for a combination of sperm density less than 20 × 10⁶/ml and motility less than 30%.

Table III

Sperm Counts of 74 Men Prior to the Start of A.I.H. Therapy with and without Pre-treatment (Irrespective of Indications of A.I.H.)

Less than 10 × 10⁶/ml	19
10-50 × 10⁶/ml	35
More than 50 × 10⁶/ml	20

Table IV

Pregnancies in the Couples according to Indications for A.I.H.

	Number of couples	Pregnancy
Low density without treatment	32	8
Low motility without treatment	11	0
Autoagglutination	2	0
Retrograde ejaculation	3	1
Kibrick greater than 1 : 64 in either partner	11	4
Kibrick less than 1 : 64 in either partner	3	2
Cervical "hostility"	13	4
Ovulation irregularity	8	2

Pregnancies occurred in several couples with more than 1 indication.

Table V

The Sperm Densities of the Males of the 19 Couples with Pregnancies

Sperm density	Numbers pregnant	Motility in pregnant couples Less than 30%	 More than 30%	Total No. of couples	%
Less than 10 × 10⁶/ml	3	1	2	19	16·6
10-50 × 10⁶/ml	10	1	9	35	28·6
More than 50 × 10⁶/ml	6	0	6	20	30·0

inseminations. In only 1 case were more than 12 inseminations carried out before a pregnancy resulted.

Of the pregnancies 13 proceeded satisfactorily beyond 28 weeks whilst 6 had spontaneous abortions in the first or early second trimester.

Discussion

A.I.H. in those selected unpromising couples has perhaps been disappointing but an initial success rate of 24% is enough to suggest that it is worth continuing with. Out of those couples achieving pregnancy many had been infertile for a long time but it should be recognised that the chance of success is small and it needs much time, effort and perseverance by staff as well as patients and the organisation of the service also requires sustained effort and enthusiasm. One way to improve the success rate would be to perform the inseminations more often around the expected time of ovulation. Thus, in Behrman's (1959) technique, long regarded as ideal, insemination was performed on 2 or 3 occasions on the days before ovulation and his success rate, like that of Russell (1960) has been greater than ours. Barwin (1974) had a 55% success rate although the sperm densities were often less than 20×10^6/ml by performing up to 6 inseminations per cycle using an intra-uterine technique.

Failures

We believe that some of our failures of A.I.H. could be explained by undiagnosed tubal obstruction, particularly in the earlier part of the series when we relied on insufflation rather than laparoscopy.

In some cases we may well have failed to detect endocrine deficiencies; thus Foldes (1972) improved his success rate by giving intravenous unconjugated oestrogen (Premarin) on the 10th, 11th and 12th day of the cycle. Now that we have access to measurements of FSH and LH, it has been possible to explain some of the failures of A.I.H. in the light of recent work by Dodson *et al.* (1975*a*) who showed lowered levels of FSH and LH in many infertile women despite apparent ovulation. This can usually be corrected by clomiphene citrate (Dodson *et al.*, 1975*b*).

In all series there is a proportion of cases who underwent A.I.H. because of cervical mucus "hostility" although this remains ill-understood and difficult to quantify.

Rumke (1975) claims that only a Kibrick titre of greater than 1 : 32 is relevant to infertility and this correlates with the findings of Ansbacher, Keung-Yeung and Behrman (1973). Isojima *et al.* (1972) suggest that the titre reflects a sperm immobilising antibody, the antigen of which they have now characterised (Isojima, Koyarna and Tsuchiya, 1974). We have found it difficult to assess its significance and our use of prednisolone has been only on a theoretical basis (Halim *et al.*, 1973*b*). In 7 out of 13 couples with a raised Kibrick titre, pregnancy resulted. It is especially difficult to assess since in 1 of our couples, the man had a titre of 1 : 640 prior to his wife's pregnancy and yet his titre fell to zero after 6 inseminations.

Macleod and Gold (1951) originally considered that a normal sperm density was above 20×10^6/ml although they subsequently modified this in the context of a varicocele to more than 15×10^6/ml. As found here and by Warner (1971) and Barwin (1974) A.I.H. gives poor results when the sperm density is less than 10×10^6/ml.

The only complications of A.I.H. in our series using the cervico-vaginal technique were few and mostly transient episodes of lower abdominal pain or intermenstrual bleeding. If an intra-uterine insemination was occasionally done then side-effects were more likely. No vaso-vagal attacks were noted. The sperm antibodies are now easily detectable but difficult to suppress. New techniques to avoid autoagglutination or reduce Kibrick titres are being tried, such as adding Hyalase and caffeine to the samples prior to insemination. The use of prednisolone was advocated in the belief that it suppressed the immune response. Freezing of sperms offers another possible improvement but if the density is less than 10 × 10^6/ml then the motility after thawing is very low even after a week's freezing. Until a new medium with improved motility has been found the technique should be used to store samples for very short times and then combined with a fresh non-frozen sample for insemination. It is a comparatively cheap technique which may well prove of the same value as in veterinary medicine as new discoveries lead to improvements.

Summary

Artificial insemination using husband's semen (A.I.H.) was carried out in 74 couples in most of whom the men had low sperm densities and/or a reduced sperm motility.

There were 19 pregnancies (24%).

The problems encountered and the reasons for failure are discussed.

We would like to express our grateful thanks to Professor J. P. Blandy and Mr G. C. Tresidder for the encouragement, advice and help in running this study. We thank Mr J. Lane for enthusiastically setting up the service and also the many members of the medical and nursing staff of both the Gynaecological and Urology Departments for their help and understanding in making the service possible.

References

Ansbacher, R., Keung-Yeung, K. and Behrman, S. J. (1973). Clinical significance of sperm antibodies in infertile couples. *Fertility and Sterility*, **24**, 305-308.

Barwin, B. N. (1974). Intrauterine insemination of husband's semen. *Journal of Reproduction and Fertility*, **36**, 101-106.

Behrman, S. J. (1959). Artificial insemination. *Fertility and Sterility*, **10**, 248-258.

Dodson, K. S., Macnaughton, M. C. and Coutts, J. R. T. (1975*a*). Infertility in women with apparently ovulatory cycles. I. Comparison of their plasma sex steroid and gonadotrophin profiles with those in the normal cycle. *British Journal of Obstetrics and Gynaecology*, **82**, 615-624.

Dodson, K S., MacNaughton, M. C. and Coutts, J. R. T. (1975*b*). Infertility in women with apparently ovulatory cycles. II. The effect of clomiphene treatment on the profiles on gonadotrophin and sex steroid hormones in peripheral plasma. *British Journal of Obstetrics and Gynaecology*, **82**, 625-633.

Foldes, J. J. (1972). Artificial insemination. *International Journal of Fertility*, **10**, 248.

Halim, A. and Antoniou, D. (1973). Autoantibodies to spermatozoa in relation to male infertility and vasectomy. *British Journal of Urology*, **45**, 559-562.

Halim, A., Antoniou, D., Leedham, P., Blandy, J. P. and Tresidder, G. C. (1973). Investigation and treatment of the infertile male. *Proceedings of the Royal Society of Medicine*, **66**, 373-378.

Isojima, S., Koyama, K. and Tsuchiya, D. (1974). The effect on fertility in women of circulating antibodies against human spermatozoa. *Journal of Reproduction and Fertility Supplement*, **21**, 125-148.

Isojima, S., Tsuchiya, K., Koyama, K., Tanaka, C., Naka, O. and Adachi, H. (1972). Further studies on sperm-immobilising antibody found in sera of unexplained cases of sterility in women. *American Journal of Obstetrics and Gynecology*, **112**, 199-207.

Kibrick, S., Belding, S. C. and Merrill, B. (1952). Methods for detection of antibodies against mammalian spermatozoa; gelatin agglutination test. *Fertility and Sterility*, **3**, 430-438.

MacLeod, J. and Gold, R. L. (1951). The male factor in fertility and infertility. II. Spermatozoon counts in 1,000 men of known fertility and 1,000 cases of infertile marriages. *Journal of Urology*, **66**, 436-449.

Rumke, P. (1975). Male Infertility Symposium, London. January 1975, in press.

Russell, J. K. (1960). Artificial insemination (husband) in the management of childlessness. *Lancet*, **2**, 1223-1225.

Warner, M. P. (1971). 500 cases of human artificial insemination—analysis of 44 years experience. *Excerpta Medica International Congress Series*, **234**, 24.

The Authors

M. McD. Usherwood, MRCOG, Senior Registrar in Gynaecology.
A. Halim, FRCS, Lecturer in Urology.
P. R. Evans, Technician, Urology Department.

British Journal of Urology (1976), **48**, 504 ©

Book Reviews

Immunological Tolerance. British Medical Bulletin. Vol. 32, No. 2. Edited by D. W. DRESSER. Pp. 86 with 16 illustrations. London: British Council Medical Dept. 1976. £3.00 in UK, £3·50 elsewhere.

This publication consists of a series of 14 separate articles on the problem of immunological tolerance. The emphasis is on fundamental mechanisms, but the application or in some cases lack of application of the findings to clinical situations is discussed.

There is inevitably some overlap in the different articles but an introduction and some concluding reflections by Dr J. H. Humphrey go a long way towards welding together the individual contributions.

For the clinician the papers make slow but enlightening reading with some acceleration of pace possible during the excellent section on organ grafting by Professor Calne. This article did, however, fail to point out the favourable outcome in renal transplant recipients with cytotoxic antibodies not cross reacting with their particular donor.

The issue is to be highly recommended to those working in the field of transplantation and in internal medicine as well as to immunologists at whom I suspect it is primarily aimed.

R. W.

Courses

INSTITUTE OF UROLOGY (UNIVERSITY OF LONDON)
In association with St Peter's Hospitals

The following seminars will be held between January and April 1977:

Infertility in the Male	15th January 1977	Fee £14
The Neuropathic Bladder Joint course with Institute of Neurology	18-19th February 1977	Fee £14
Operative Surgery for the FRCS	12th March 1977	Fee £9
Urological Oncology	22-23rd April 1977	Fee £14

Applications to the Secretary, Institute of Urology, 172 Shaftesbury Avenue, London WC2H 8JE, from whom detailed programmes may be obtained.

ABSTRACTS FROM CURRENT UROLOGICAL LITERATURE

Deutsche Medizinische Wochenschrift

By John Grieve

"Nephrectomy for Hypertension in Older People with Unilateral Renal Disease." W. Wagner and F. Boeminghaus. (1975), **100**, 355-357.)—Between 1961 and 1972 42 patients aged more than 40 at the time of operation had a nephrectomy for hypertension related to unliateral renal disease. These patients have recently been re-examined using the W.H.O. criteria for normality and hypertension. In 15 patients systolic and diastolic pressures returned to normal, while in 12 no change occurred. The good results occurred in those with small pyelonephritic kidneys while those with pyelonephritis in normal-sized kidneys, arteriosclerosis and renal artery stenosis showed no benefit. The authors conclude that patients over 40 with hypertension related to unilateral renal disease are most likely to benefit from nephrectomy if they have a small pyelonephritic kidney.

"The Optimum Time for Treatment of Undescended Testis." J. Ludwig and J. Potempa. (1975, **100**, 680-683.)—In this Heidelberg clinic 133 patients were operated on for undescended testis in the years 1950-60. Of these, 102 were traced for follow-up, but only 79 were examined. Unilateral maldescent occurred in 71 and bilateral in 8. Those with bilateral non-descent produced no children while, in the 71 with the unilateral condition, fertility appeared greatest in those operated on in the first or second year of life. The authors conclude (without too obvious justification) that the optimum time for operation is, at the latest, the second year of life.

"Autologous Renal Transplantation in Renovascular Hypertension." F. Piza, W. K. Waldhäusl and H. Czembirek. (1975, **100**, 1177-1183.)—In a 20-year-old man renovascular hypertension was apparently due to bilateral renal artery stenosis and infrarenal aortic coarctation. Reconstruction of the renal arterial supply with vein grafts and aortorenal bypass did not reduce the blood pressure. Bilateral renal autotransplantation to the iliac fossae and a dacron lay-on graft for the coarctation gave a normal pressure. The authors consider that plasma renin concentration in the renal vein and the patients' age are of prime importance in deciding on reconstructive surgery for renal artery stenosis.

"New Chemotherapy (Adriamycin, Bleomycin and Vinicristine) in Metastasising Testicular Teratoma." S. Seeber, W. M. Gallmeier, K. Höffken, R. Osieka, U. Bruntsch and C. G. Schmidt. (1975, **100**, 1319-1324.)—In a prospective study 16 out of 18 patients were fully assessed. All were treated with Adriamycin, Bleomycin and Vincristine and 12 were stage IV, 3 stage III and 1 stage II. The side effects in 12 patients were not severe enough to necessitate in-patient treatment. The low toxicity and good remissions suggest that this combination of drugs gives better results than Actinomycin D on its own.

La Nouvelle Presse Médicale

By John Grieve

"Recurrent Calcium Nephrolithiasis and Parathormone." J. Berheim, L. David, N. Pozet, P. Zech, H. My and J. Traeger. (1975, **4**, 1913-1916.)—These authors from Lyons examined the peripheral parathormone level in 25 cases of recurrent renal calculi using radioimmune assay to detect minimal hypersecretion of parathormone. In only 1 patient was there an abnormal result after a stimulation test with calcium infusion. This took the form of a secondary rebound phenomenon involving the parathormone level. The conclusion was that these tests are of very limited value in detecting minimal hyperparathyroidism.

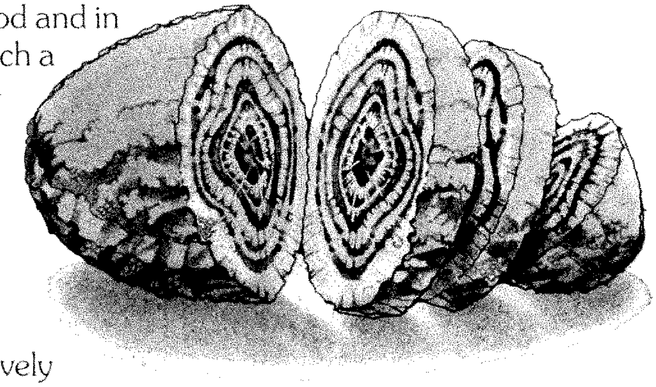
Printed in Great Britain by T. & A. Constable Ltd, *Hopetoun Street, Edinburgh*

Diet and renal stones. The inside story.

Traditionally, patients with idiopathic hypercalciuria have been treated with a low calcium diet.

Indeed, "A diet with a very low calcium content, less than 50 mg daily, should provide an effective method of controlling calciuria."[1]

However, "due to the presence of calcium in so many kinds of food and in drinking water, such a diet is hardly possible. It is not palatable and would lack many indispensable trace elements."[1] Many foodstuffs contain a deceptively high level of calcium. A meal consisting of lamb stew can yield more calcium than the recommended allowance.[2]



This is why Whatman Sodium Cellulose Phosphate is being used increasingly as adjunctive treatment for idiopathic hypercalciuria. Whatman Sodium Cellulose Phosphate reduces calcium absorption and prevents renal stone formation.[3]

1. *Brit J Urol*, (1973), **45**, 136.
2. *Composition of Foods*, (1960), MRC Report 297, HMSO, London.
3. *American J Med*, (1971), **50**, 67.

Whatman®

Sodium Cellulose Phosphate

Fundamental treatment for idiopathic hypercalciuria.

Further information and data sheet on request from Whatman Biochemicals Limited, Springfield Mill, Maidstone, Kent ME14 2LE. Telephone: Maidstone 673841. Telex: 96113.

® Registered trade mark of Whatman Limited

0651

UNIVERSITY OF OTAGO *Faculty of Medicine*
CHRISTCHURCH CLINICAL SCHOOL *Christchurch, New Zealand*

lecturer or senior lecturer in urology

Applications are invited for the position of Lecturer or Senior Lecturer in Urology in the University Department of Surgery at the Christchurch Clinical School. Applicants must be competently trained clinical urologists and furnish clear evidence of their ability to engage successfully in unsupervised scientific enquiry. It is hoped that the successful applicant will take up his duties during or at the end of 1977.

Specific enquiries related to the appointment may be addressed to Professor W. A. A. G. Macbeth of the Department of Surgery, Christchurch Clinical School, Christchurch Hospital, Private Bag, Christchurch, New Zealand.

Salary: Lecturer: $NZ11,407–$NZ15,932 per annum with a bar at $NZ13,309 per annum
Senior Lecturer: $NZ16,369–$NZ18,730 per annum

An allowance for clinical duties may be available in the light of status and duties performed.
(Note: $NZ100 equals approximately £55 sterling; $US100)

Further particulars are available from the Secretary-General, Association of Commonwealth Universities (Appointments), 36 Gordon Square, London WC1H 0PF or from the undersigned.

Applications quoting reference A.76/63 close in New Zealand and London on *31 January 1977.*

D. W. GIRVAN *Registrar*

JOURNAL OF PATHOLOGY

A Journal of the Pathological Society of Great Britain and Ireland

Edited by W G Spector

The Journal of Pathology was first published as the Journal of Pathology and Bacteriology in 1892. The articles printed are concerned with experimental pathology, morbid anatomy and comparative pathology. They are intended in the main for practising medical pathologists, though they are often of interest to those working in other fields; a fairly extensive knowledge of pathology is therefore assumed in most of them.
Other contents include reviews of books, accounts of the proceedings of the Society, and obituaries of deceased members.

Published monthly. Four parts complete a volume.

Volumes 121, 122, 123, 1977

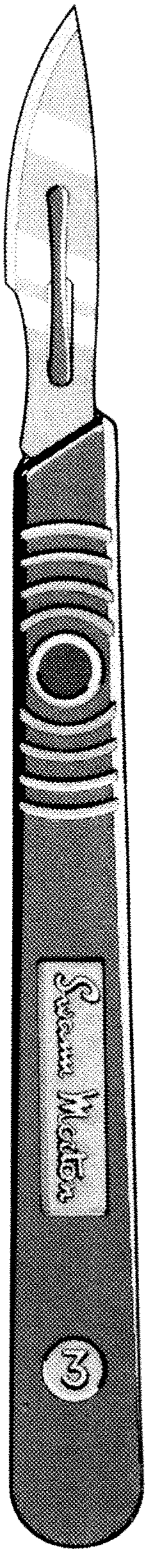
Annual subscription £30.00 USA $72.00

Single numbers £3.00 USA $7.50

Subscription enquiries to: Longman Group Ltd., Journals Division, 43-45 Annandale Street, Edinburgh EH7 4AT

All orders must be accompanied by the appropriate remittance.

Longman



The best scalpel.

Anyone who's ever used a scalpel knows the name of Swann Morton.

The makers of the best surgical blades in the world. A name that guarantees the highest quality possible.

Sterilized Carbon Steel Blades. Sterilized Stainless Steel Blades. Standard Carbon Steel Blades. Sterile Disposable Stitch Cutters. Surgical Handles.

Swann-Morton

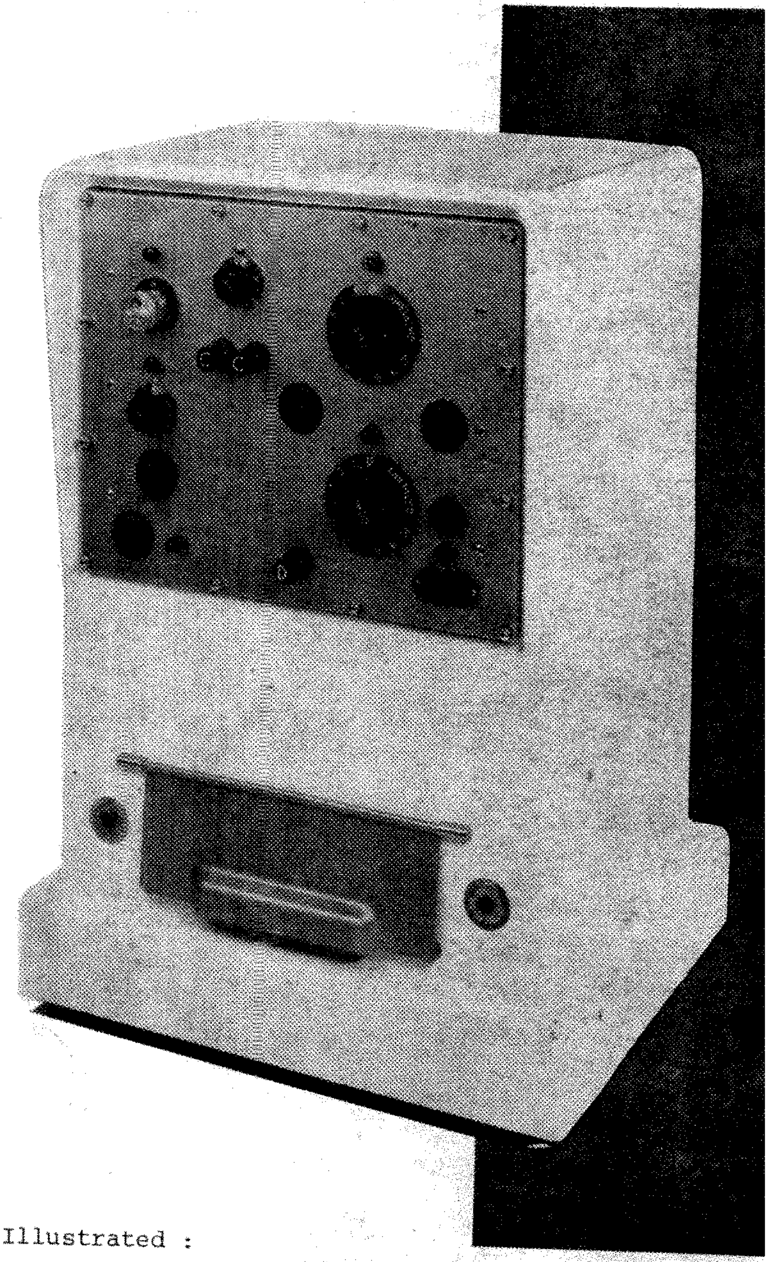
SWANN MORTON LIMITED
PENN WORKS,
OWLERTON GREEN,
SHEFFIELD S6 2BJ, ENGLAND.

We know what you want!

AFTER MORE THAN 50 YEARS SERVING THE NEEDS OF UROLOGISTS WE REALISE THAT A RESECTOSCOPE IS ONLY AS GOOD AS THE DIATHERMY MACHINE.

WE KNOW YOU WANT RELIABLE, SAFE, SMOOTH, POWERFUL BUT CONSISTENT CUTTING AND COAGULATING.

WE KNOW YOU WANT EXPERT, FAST SERVICING IN THE EVENT OF A BREAKDOWN.



Illustrated :

Turner-Warwick Urological Unit with spark gap and valve circuits with blender, including fibre light and cautery. GU332A/FLC.

We have what you want

et us send you our new Catalogue
our complete Diathermy range.

GU MFG. CO. LTD.
Plympton St., London, NW.8.

ISSN 0007-1

BRITISH JOURNAL OF UROLOGY

EDITOR
* W. KEITH YEATES

HON. TREASURER
* C. H. KINDER

ASSISTANT EDITORS
* G. D. CHISHOLM
* D. M. ESSENHIGH
* W. F. HENDRY
* W. SELBY TULLOCH

ASSISTANT EDITOR FOR AUSTRALASIA
G. F. MURNAGHAN

CONSULTING EDITORS
* DAVID BAND
* J. D. FERGUSSON

EDITORIAL COMMITTEE
Chairman D. INNES WILLIAMS*

M. HANDLEY ASHKEN, Norwich
G. H. BAINES, Birmingham
JOHN BALFOUR, Vancouver
D. R. BARNES, Cape Town
*J. P. BLANDY, London
JEAN CHARBONNEAU, Montreal
C. A. C. CHARLTON, Bath
PHILIP CLARK, Leeds
B. N. COLABAWALLA, Bombay
M. H. DEVEREUX, Loughton, Essex
J. N. de KLERK, Cape Town
E. CHARLTON EDWARDS, Manchester
E. J. ENGLAND, Perth, W. Australia
H. FINE, Durban
ALBAN H. GEE, Sydney
N. O. K. GIBBON, Liverpool
JOHN GRIEVE, Dundee
A. R. HARRISON, London
D. K. KARANJAVALA, Bombay
J. A. KENNEDY, Belfast
W. K. KERR, Toronto
KENNETH J. MACKINNON, Montreal
J. W. F. MACKY, Auckland
JOHN P. MADDERN, Adelaide
*J. P. MITCHELL, Bristol
*RICHARD A. MOGG, Cardiff
J. DERMOT O'FLYNN, Dublin
H. H. PEARSON, M.B.E., Canberra
J. S. PETERS, Melbourne
R. C. B. PUGH, London
P. J. M. RETIEF, Cape Town
CHARLES J. ROBSON, Toronto
L. STUART SCOTT, Glasgow
K. E. D. SHUTTLEWORTH, London
SARINDER MAN SINGH, Delhi
J. C. SMITH, Oxford
J. J. STEVENSON, London
*J. H. STEYN, Aberdeen
W. BARR STIRLING, Glasgow
JOHN SWINNEY, M.C., Bunbury, W. Australia
G. C. TRESIDDER, London
P. J. P. VAN BLERK, Johannesburg
DAVID M. WALLACE, O.B.E., London
J. G. WATSON, Brisbane
R. H. WHITAKER, Cambridge
*J. L. WILLIAMS, Sheffield
J. F. R. WITHYCOMBE, Cambridge
P. H. L. WORTH, London

* Members of Executive Committee

ST PETER'S MEDAL AWARDED TO

J. B. MACALPINE, 1949
R. OGIER WARD, 1951
TERENCE J. MILLIN, 1951
A. CLIFFORD MORSON, 1954
LESLIE N. PYRAH, 1959
CUTHBERT E. DUKES, 1960
DAVID BAND, 1962
SIR ERIC RICHES, 1964
ARTHUR H. JACOBS, 1965
D. INNES WILLIAMS, 1967
H. HAMILTON STEWART, 1968
JOHN SWINNEY, 1969
SIR MICHAEL WOODRUFF, 1970
D. S. POOLE-WILSON, 1971
DAVID M. WALLACE, 1973
A. W. BADENOCH, 1974
HOWARD G. HANLEY, 1975

E. & S. Livingstone
Edinburgh and London
BAUS 1976

Contents

PAPERS READ AT THE 32nd ANNUAL MEETING OF THE BRITISH ASSOCIATION OF UROLOGICAL SURGEONS IN LONDON, JUNE 1976

507 **The Management of the Patient with Calcium Stones**
E. R. Yendt and M. Cohanim

515 **Crystalluria in Normal Subjects and in Stone Formers With and Without Thiazide and Cellulose Phosphate Treatment**
P. C. Hallson and G. Alan Rose

525 **Size of Renal Calculi, Recurrence Rate and Follow-up**
John P. Blandy and Villis R. Marshall

531 **Recurrence of Infected Calculi Following Postoperative Renal Irrigation with Stone Solvent**
Gavin Royle and Joe C. Smith

539 **Primary Hyperparathyroidism—A Review of Cases in the Sheffield Area**
J. C. Hammonds, J. L. Williams and L. Harvey

549 **Primary Pelvic Hydronephrosis in Children: A Retrospective Survey**
Patrick Smith, Michael Roberts, Robert H. Whitaker and Abdel Raouf Garousche

555 **Reflux Induced Pelvi-ureteric Obstruction**
Robert H. Whitaker

561 **Occupational Bladder Tumour Cases Identified During Ten Years' Interviewing of Patients**
Joan M. Davies, Sheena M. Somerville and D. M. Wallace

567 **Inverted Papillomas of the Lower Urinary Tract**
Katherine M. Cameron and Charles H. Lupton

579 **The Value of Lymphography in the Management of Bladder Cancer**
A. G. Turner, W. F. Hendry, J. S. Macdonald and D. M. Wallace

587 **The Management of Deeply Infiltrating (T_3) Bladder Carcinoma: Controlled Trial of Radical Radiotherapy versus Preoperative Radiotherapy and Radical Cystectomy (First Report)**
D. M. Wallace and H. J. G. Bloom

595 **Radiotherapy in the Treatment of Recurrent Bladder Cancer**
W. D. Rider and D. H. Evans

603 **Hyperthermia in the Treatment of Bladder Tumours**
R. R. Hall, V. Wadehra, J. M. Towler, J. R. Hindmarsh and P. O. Byrne

609 **Treatment of Advanced Bladder Cancer with Adriamycin and 5-Fluorouracil**
R. J. Cross, R. W. Glashan, C. S. Humphrey, M. R. G. Robinson, P. H. Smith and R. E. Williams

617 **The Endemic Bladder Stones of Indonesia—Epidemiology and Clinical Features**
Kamardi Thalut, Ahmad Rizal, J. G. Brockis, R. C. Bowyer, T. A. Taylor and Z. S. Wisniewski

ISSN 0007-1331

The best scalpel.

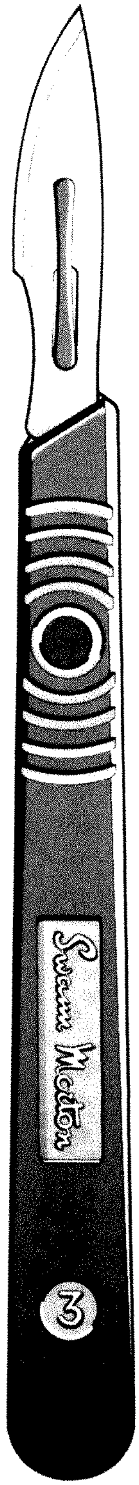
Anyone who's ever used a scalpel knows the name of Swann Morton.

The makers of the best surgical blades in the world. A name that guarantees the highest quality possible.

Sterilized Carbon Steel Blades. Sterilized Stainless Steel Blades. Standard Carbon Steel Blades. Sterile Disposable Stitch Cutters. Surgical Handles.

Swann-Morton

SWANN MORTON LIMITED
PENN WORKS,
OWLERTON GREEN,
SHEFFIELD S6 2BJ. ENGLAND.



623 **Distension Therapy for the Unstable Bladder: Later Results including an Assessment of Repeat Distensions**
P. D. Ramsden, J. C. Smith, M. Dunn and G. M. Ardran

631 **Clinical and Experimental Studies on the Action of Prostaglandins and their Synthesis Inhibitors on Detrusor Muscle *in vitro* and *in vivo***
M. I. Bultitude, N. H. Hills and K. E. D. Shuttleworth

639 **Anti-reflux Surgery in the Congenital Neuropathic Bladder**
J. H. Johnston, S. R. Shapiro and G. G. Thomas

643 **The Assessment of Sphincteric Activity in Patients following Trans-sphincteric Urethral Reconstruction**
Robert D. Schwarz, John W. Foote, Douglas D. Morehouse and Kenneth J. Mackinnon

649 **Division of the External Urethral Sphincter in the Neuropathic Bladder: A Twenty Years' Review**
J. Cosbie Ross, N. O. K. Gibbon and G. Sham Sunder

657 **An Assessment of Surgical Treatment of Vesical Outlet Obstruction in Spinal Cord Injury: A Review of 471 Cases**
J. Dermot O'Flynn

663 **Urodynamics in the Prune Belly Syndrome**
H. M. Snyder, N. W. Harrison, H. N. Whitfield and D. Innes Williams

671 **Anterior Detrusor Tube Repair for Urinary Incontinence in Children**
D. Innes Williams and Howard Snyder

675 **A Simple Artificial Implantable Sphincter**
Michael Rosen

681 **Excretion Urography in the Investigation of Prostatism**
P. H. Abrams, J. Roylance and R. C. L. Feneley

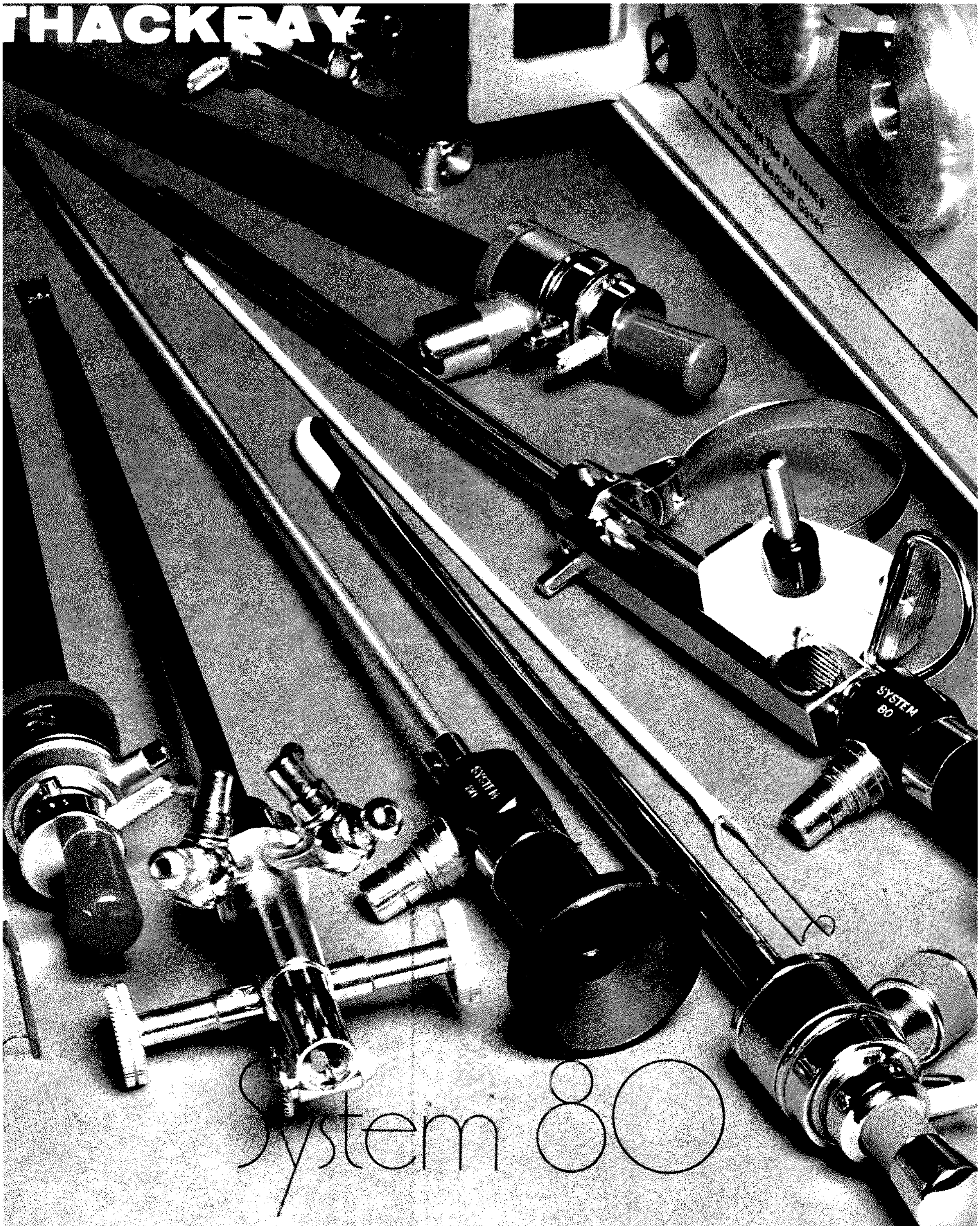
685 **Hypothermic Prostatic Resection**
A. Serrao, M. K. Mallik, P. A. Jones, W. F. Hendry and J. E. A. Wickham

689 **Lymphography and Pelvic Lymphadenectomy in Carcinoma of the Prostate**
E. P. N. O'Donoghue, P. Shridhar, T. Sherwood, J. P. Williams and G. D. Chisholm

697 **Urethroplasty in Context**
J. P. Blandy, S. Wadhwa, M. Singh and G. C. Tresidder

703 **Hypospadias—Problems of Postoperative Fistulae Formation and a Modified 2-Stage Procedure to Reduce These**
P. J. B. Smith, P. L. G. Townsend, R. W. Hiles and J. R. Bryson

709 **Plasma Gonadotrophic Hormones, Testicular Biopsy and Seminal Analysis in the Men of Infertile Marriages**
J. P. Pryor, R. C. B. Pugh, K. M. Cameron, J. R. Newton and W. P. Collins



A modular range for examination, catheterisation and resection.
The system is built around the clarity of a rod lens telescope and manufactured to B.A.U.S. specification in accordance with patent number 954 629.

A well proven 24 hours telescope repair service is available in the U.K. when necessary.

For further information please contact: Chas. F. Thackray Limited.

Instructions to Authors

The *British Journal of Urology* welcomes original contributions on urological subjects from all parts of the world. The papers are accepted for consideration on the understanding that their contents have not been published in whole or in part elsewhere and that they are subject to editorial revision.

Any paper may be sent initially to a member of the Editorial Committee for comment and advice on its being suitable to be considered for publication.

A leaflet showing the criteria used in the assessment of papers submitted for consideration is available from the Editor on request.

Authors should supply their qualifications, main appointment, and the name and address of the hospital or the laboratory.

Please indicate name and address to which requests for offprints should be made.

Format and content of papers

The text of articles submitted for publication should be typewritten in double-spacing on paper sheet size 22 × 32 cm (A4). There should be a minimum margin of 3 cm all round. The pages should be numbered.

Reports on clinical or laboratory investigation should as far as possible be organised into the following main sections: (1) Introduction, (2) Objective(s), (3) Patients or Materials, (4) Procedures or Methods, (5) Findings or Results, (6) Discussion and (7) Conclusions with (8) a Summary at the end.

Nephrology. Papers on disorders of renal function of interest to the urological surgeon are welcome.

Ethics. When relevant, authors must include a statement on the ethical aspects of their research.

Reports of clinical cases should consist of the following sections: (1) Introduction, (2) Case Reports and (3) Comment with (4) a Summary at the end.

Reports on single cases. Papers reporting a single case are considered for publication as full papers only when the case has definite instructional value. The Introduction and Discussion should not be disproportionate to the case presentation. *An abbreviated version suitable for publication as a Short Case Report as an alternative must also be submitted.*

In all full papers the literature should be summarised as concisely as is consistent with establishing the necessary basis for new material. Discussion and Conclusions should be strictly limited to the results presented. Recapitulation from previous sections should be avoided whenever possible. Summaries should be composed of very brief statements about each of the main sections.

Headings. The relative importance of sub-headings should be clearly indicated.

Numbers. All numbers should be shown as figures rather than as words.

References. *The accuracy of references is the responsibility of the author.* Only papers closely related to the author's work should be referred to; exhaustive lists should be avoided. *References ~~in the~~ text* should be quoted by the author's name(s) and year of publication. Unless there are more than 3 authors, all the names should be stated at the first reference; if there are more than 3 authors only the first author plus *et al.* is used. In subsequent references to the same paper, *et al.* is used if there are more than 2 authors. *The list of references at the end of the paper* should be in alphabetical order. *References to Journals* should include the name(s) and initials of the author(s), year, title of paper, name of journal in full, volume number and the numbers of the first and last pages, *References to books* should include the name and initials of the author, year, title of book, number of edition, city of publication, name of publishing house, and page number(s).

Illustrations. Photographs and radiographs should be submitted in the form of *matt* prints of a size no larger than 17·5 × 12·5 cm and no smaller than 9 × 6·5 cm. All figures should be sent unmounted. The number of the figure, the name of the author and the "top" of the illustration should be indicated lightly in pencil on the back. The magnification of micro-photographs should be stated. Graphs and diagrams should be drawn in Indian ink. *Lettering and figures must be indicated only on a transparent cover.* Legends to figures should be typewritten on a separate sheet of the manuscript. Tables, unless they are very small, should also be typewritten on separate sheets. The position of illustrations and tables should be indicated in the margin of the text.

There is no charge to contributors for the printing of black-and-white illustrations on papers accepted for publication. Illustrations in colour may be accepted at the discretion of the Editor provided he is of the opinion that these are necessary for the improvement of the article. The author may be required to pay for the extra cost involved by the reproduction in colour.

Offprints

25 offprints are supplied to the first named author only, free. Forms for ordering offprints will be sent with the proofs for correction; the order form should be returned with the corrected proofs within 7 days.

Continued on page vii

THACKRAY

The Raper Cystoscopy and X-ray trolley designed for all routine procedures in the Cystoscopy Clinic from examination to recovery, and for any situation where the patient is examined in the lithotomy position. Patent No. 1050834.

For further information please contact:

Travelling Fellowship

The British Association of Urological Surgeons offers a Travelling Fellowship of £250 based on the best paper published in the *British Journal of Urology* in the preceding year including those papers presented at the British Association of Urological Surgeons Annual Meeting.

Candidates for the prize must be Fellows of one of the Royal Colleges of Surgeons in the British Isles, Canada, Australasia or South Africa who are in the course of urological training or who have obtained consultant posts within 10 years of the date of submission of the paper.

Authors of papers with multiple authorship should indicate which one of their number should be awarded the Fellowship in the event of their contribution being selected.

Three assessors will be appointed by the Council to make recommendations on the award of the Fellowship. The Council reserves the right not to make an award in any one year.

The award will be announced at the June meeting of the Association.

Short Case Reports

Brief reports (preferably with 1 and not more than 2 illustrations) of unusual cases not published elsewhere may be submitted as summaries of not more than 200 words for consideration for publication as Short Case Reports. They should comprise (1) a Title, (2) Case description and (3) a brief Comment. The authors and references are each limited to 3. The titles of these reports will usually be recorded in Index Medicus and by MEDLARS.

Preliminary Communications

Preliminary communications of original work may be submitted as short papers. The communication should be divided into 4 sections: (1) Objectives, (2) Materials and Methods, (3) Preliminary results, (4) Interpretation or Significance of Results.

Discussion of Papers

Questions or criticisms concerning recently published papers' may be sent to the Editor, who will refer them to the authors. The readers' comments and authors replies may subsequently be published together.

There is no other correspondence section in the Journal.

Suggested Projects for Urological Research

Clinicians who have ideas for research projects, but have no opportunity for carrying them out, may submit them for publication in the above section. The communication should not be longer than 500 words. References will be limited to 6.

Abstracts from Current Urological Literature

Urologists who are willing to undertake abstracting of urological articles appearing in other journals should communicate with the Assistant Editor, Mr. W. Selby Tulloch, at the Department of Urology, Western General Hospital, Edinburgh, EH4 2XU.

Addresses

With the exceptions noted below, all editorial communications, including books for review, should be addressed to the Editor. Mr. W. Keith Yeates, at the Department of Urology, Newcastle General Hospital, Newcastle upon Tyne, NE4 6BE.

Preliminary Communications on Research Projects and *Suggested Projects for Urological Research* should be submitted to the Assistant Editor, Mr G. D. Chisholm, at the Urology Unit, Hammersmith Hospital, Royal Postgraduate Medical School, London, W12 0HS.

Short Case Reports (presented as described above) should be sent to the Assistant Editor, Mr W. F. Hendry, Institute of Urology, University of London, 172 Shaftesbury Avenue, London, WC2H 8JE.

Communications concerning the Abstract Section should be sent to the Assistant Editor, Mr W. Selby Tulloch, at the Department of Urology, Western General Hospital, Edinburgh, EH4 2XU.

Publishing, Advertisement and other enquiries: E. & S. Livingstone, Longman Group Ltd., Journals Division, Longman House, Burnt Mill, Harlow, Essex CM20 2JE.

Subscriptions

The Journal is published in February, April, June, August, October and December. Volume 48, number 7, is included in the subscription price and publishes the papers presented at the 1976 B.A.U.S. Conference. Subscription £17·00 (U.S.A. $45.00) per annum, post free. Single copies £3·00 (U.S.A. $7.50) each. Previous volumes and parts of volumes (if available) may be obtained from the publishers, price £6.00 per volume or 75p for single parts.

Subscription enquiries: Messrs E. & S. Livingstone, Journals Division, 43/45 Annandale Street, Edinburgh, EH7 4AT.

Subscriptions for U.S.A. should be sent to The Williams and Wilkins Company, 428 East Preston Street, Baltimore, Maryland, U.S.A.

© 1976. All rights reserved. No part of this publication may be reproduced, stored in a retrieval system, or transmitted in any form or by any means, electronic, mechanical, photo-copying, recording or otherwise, without the prior permission of the copyright owner.

EPTRIN
n urinary infections

e clinical superiority that makes sure

study of the sensitivities of acute urinary infection isolates ommonly-used oral antibacterials, 99·1% of the pathogens ated were sensitive to Septrin[1].

trin* has a complete spectrum of activity against the nisms usually responsible for urinary tract infections. With actericidal action, speed of patient response and con- ient dosage, Septrin has become the most widely-used acterial for treating urinary infections.

t. med Res (1974), **2** 400

in contains trimethoprim and sulphamethoxazole.
rescribing information is available on request.
ome Medical Division. The Wellcome Foundation Ltd., Berkhamsted, Herts
Mark

Wellcome

In Radiography Conray contrast media

A comparatively broad and subjective view

'Conray' Contrast Media offer a comparatively wide choice of formulations spanning the requirements of precision, safety and economy together with superior visualization in a broad range of radiodiagnostic procedures. There is almost certainly a 'Conray' formulation precisely suited to your requirements however exacting they may be.

'Conray' Contrast Media are preparations of meglumine iothalamate, sodium iothalamate or combinations of the two.

Further information on 'Conray' 280, 'Conray' 325, 'Conray' 420, Cardio-'Conray', Retro-'Conray' and Gastro-'Conray' supplied on request.

'Conray' is a trade mark of Mallinckrodt Inc.

May & Baker Ltd Dagenham Essex RM10 7XS

M&B May&Baker A member of the Rhône-Poulenc Group of Companies

MA 5184

An Excerpta Medica Abstract Journal

urology and nephrology

about 4,000 current abstracts in 10 fully indexed issues a year.

All abstracts are classified under the following headings:

1 General and experimental aspects
2 Urological instruments
3 Kidney
4 Renal pelvis
5 Ureter
6 Bladder and urachus
7 Urinary diversion
8 Prostate and seminal vesicles
9 Urethra and glans penis
10 Penis
11 Scrotum and scrotal contents
12 Intersexuality
13 Infertility
14 Adrenal glands; Retroperitoneum
15 Chemical injuries
16 Renal physiology
17 Stone formation
18 Diagnostic procedures
19 Urinary tract infections
20 Genitourinary tuberculosis
21 Parasitic disease
22 Hypertension
23 Renal failure
24 Dialysis
25 Renal transplantation
26 Glomerular disease
27 Tubular disorders
28 Nephrotic syndrome
29 Renal aspects of general disorders
30 Urological aspects of general disorders
31 Pharmacology and medical treatment
32 Venereal diseases

Annual subscription rate: US$ 116.95/Dfl. 292.00 postage included.

Quotations on back volumes will be provided on request.

The Dutch Guilder price is definitive.

excerpta medica
P.O. Box 211 - Amsterdam - The Netherlands

5320 EM

New Stomahesive™ Flanges!

Giving confidence in a secure appliance, maximum skin protection and the comfort of Stomahesive.

Available in sizes:
32 mm (1¼″), 38 mm (1½″), 45 mm (1¾″)

A natural addition to the Stomahesive range.

Stomahesive flanges enhance the benefits of two-piece appliances.

Further information available from
E. R. SQUIBB & SONS LTD, Regal House, Twickenham TW1 3QT

SQUIBB
Stoma care

MEDICAL AND BIOLOGICAL ILLUSTRATION

The Journal of the Institute of Medical and Biological Illustration

Edited by Richard Morton

Medical and Biological Illustration is a journal that covers the use of all audio-visual media used for the practice, research, and teaching of medicine and other life sciences. From the producer's point of view the Journal is, therefore, of interest to artists, graphic designers, photographers, cinematographers, television personnel, audio specialists, educational technologists. The Journal reports the work they are doing in their own particular speciality, and is an important means of keeping them up to date. In such a multidisciplinary subject as illustration a common forum helps to solve common problems.

The users of communication media either as teachers, research workers, writers, or publishers find Medical and Biological Illustration not only a useful contact with producers, but also a vehicle in which to publish their own results on the use of audio-visual techniques in their own particular fields. This ability to bring together producer and user continues to be one of the most important functions of the Journal. This is achieved through original contributions, abstracts from the literature, book reviews, and notes on new equipment and methods. This is the only Journal in any language which consistently covers at an international level all aspects of design, production, application, and evaluation of all the different media in the medical and biological sciences.

Published quarterly in February, May, August and November

Volume 27, 1977

Annual subscription	£10.00	USA $24.00
Single numbers	£3.00	USA $7.50

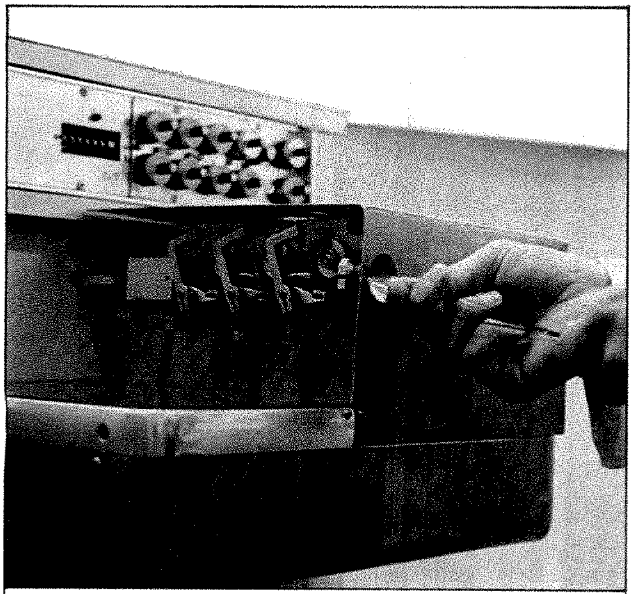
Subscription enquiries to: Longman Group Ltd., Journals Division,
43/45 Annandale Street, Edinburgh. EH7 4AT

All orders must be accompanied by the appropriate remittance.

Longman

HE CHALLE
OF SUTURES

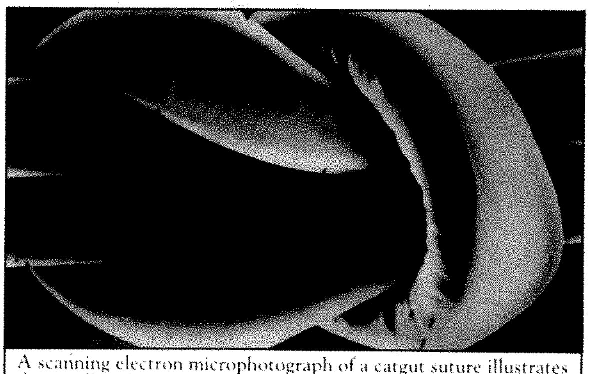
ABSORBABLE DEVELOPMENTS



Controlling the diameter of a catgut suture at every point along the strand.

An absorbable suture which is uniform and will pass smoothly through even delicate tissue is essential in many areas of surgery. Whilst catgut is an established product ETHICON* have long pursued a programme of development to improve its surgical performance.

A special polishing process now produces an exceptionally smooth catgut suture that varies in diameter less than two ten thousandths of an inch along its entire length. The smooth surface finish greatly improves its passage through tissue, whilst narrow manufacturing tolerances ensure uniform strength and predictable performance.



A scanning electron microphotograph of a catgut suture illustrates the excellent knotting properties of this material.

MEETING THE CHALLENGE

Suture requirements and wound closure techniques are constantly subject to re-evaluation and change. At ETHICON we are very much a part of this process and welcome the challenge it offers. We put our considerable research, development and manufacturing resources to work to produce still better needle designs and suture materials.

ETHICON
TRADEMARK
SERVICE TO SURGERY

JOURNAL OF PATHOLOGY

A Journal of the Pathological Society of Great Britain and Ireland

Edited by W G Spector

The Journal of Pathology was first published as the Journal of Pathology and Bacteriology in 1892. The articles are concerned with experimental pathology, morbid anatomy and comparative pathology. They are intended in the main for practising medical pathologists, though they are often of interest to those working in other fields; a fairly extensive knowledge of pathology is therefore assumed in most of them. Other contents include reviews of books, account of the proceedings of the Society, and obituaries of deceased members.

Published monthly, Four parts complete a volume.

Volumes, 121, 122, 123, 1977

Annual subscription	£30.00	USA $72.00
Single numbers	£3.00	USA $7.50

Subscription enquries to: Longman Group Ltd., Journals Division,
43/45 Annandale Street, Edinburgh. EH7 4AT

All orders must be accompanied by the appropriate remittance.

Longman

AN IMPORTANT ANNOUNCEMENT FROM MAY & BAKER:

A MAJOR, NEW INDICATION FOR 'FLAGYL'

the treatment and prevention of anaerobic infections

Modern methods reveal the size of the problem

Sophisticated laboratory techniques now show the true incidence of anaerobic infections. Increasingly, these organisms are isolated from clinical specimens,[1] and are implicated in a wide variety of infections.[1-3]

'FLAGYL' is the dependable answer

Free from the problems associated with other agents in this field (eg chloramphenicol) and, unlike penicillin, active against both sporing and non-sporing forms – 'Flagyl' is bactericidal to most of the clinically important, obligatory anaerobes.[1] 'Flagyl' has been used successfully in the following conditions: pelvic,[4] intra-abdominal[5] and post-operative[4] infections, brain abscess[6] septic thrombophlebitis[7] and necrotizing pneumonia.[8]

Positive benefits to the hospital unit

". . . it may be concluded that the prophylactic use of metronidazole ('Flagyl') in the test group resulted in a saving to the N.H.S. of almost £2,000 . . . prevention of anaerobic infection enabled the gynaecological ward to handle an additional 26 major surgical cases each year."[4]

Backed by an unrivalled reputation

'Flagyl' has an outstanding record of efficacy and safety in over 15 years of clinical experience. It is now firmly established in the treatment of urogenital trichomoniasis, amoebiasis, giardiasis and acute ulcerative gingivitis.

References

1. *Drug and Therapeutic Bulletin*, **14**, 25, 1976
2. Phillips, I. and Sussman, M. p.37 *Infections with Non-Sporing Anaerobes* Published Churchill
3. Study group, *Lancet*, **ii**, 1540, 1974
4. Study group, *J. Antimicrobial Chemotherapy*, **1**, 393–401, 1975
5. Willis, A.T., *et al., Br.Med.J.*, February 7, **i**, 318–321, 1976
6. Ingham, H.R., *et al., Br.Med.J.*, **iv**, 39, 1975
7. Mitre, R.J. & Rotheram, E.B., *J.Amer.Med.Assoc.*, **230**, 1168, 1974
8. Tally, F.P., *et al., Antimicrobial Agents & Chemotherapy*, **7**, 672, 1975

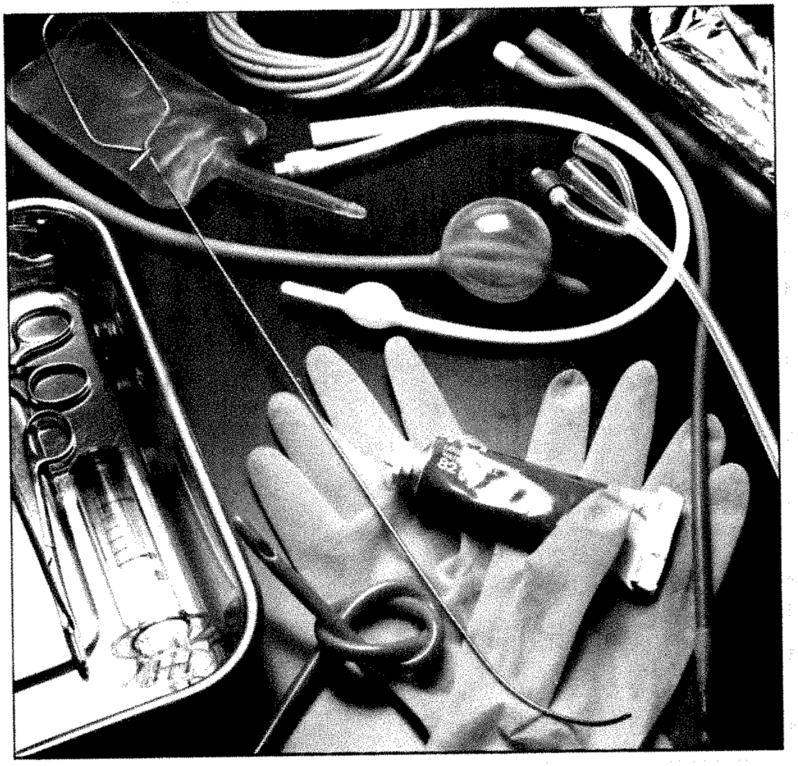
'Flagyl'* is supplied as tablets of 200 mg and tablets of 400 mg. Full prescribing information on request
*trade mark of May & Baker Ltd Dagenham Essex RM10 7XS for its preparations of metronidazole.

M&B May & Baker

A member of the
Rhône-Poulenc Group of Companies

MA4576

THE POSTOPERATIVE PATIENT'S
NIGHTMARE...



URINE RETENTION
INTESTINAL ATONY

THE GENTLE ALTERNATIVE . . . UBRETID® (DISTIGMINE BROMIDE)
Gently restores bladder tone. Progressively reactivates intestinal motility. Offers an alternative to catheterisation: minimises risk of Urinary Infection. Lowers residual urine volumes. 24-hour action: once-a-day dosage. Tablet and Injectable formulations.

UBRETID® – GENTLY RESTORES MUSCLE TONE
Full prescribing information is available on request

Berk Pharmaceuticals Limited
Shalford, Surrey
® Registered Trade Mark
J4942

British Journal of Urology (1976), **48**, 507-514 ©

The Management of the Patient with Calcium Stones[1]

E. R. YENDT and M. COHANIM

Department of Medicine, Kingston General Hospital and Queen's University, Kingston, Ontario, Canada

During the past 8 years we have investigated approximately 800 patients with kidney stones in Kingston. There are 3 aspects of this study which we wish to emphasise. First, all biochemical determinations have been performed in our own research laboratory. Second, our studies have been performed while our patients were eating their usual diets and whenever possible 24-hour urine specimens have been collected on an out-patient basis rather than in hospitalised patients. Our preference for out-patient studies is based on a series of approximately 70 patients in whom 24-hour urine collections were made initially during hospitalisation and subsequently as out-patients (on *ad libitum* diets). In those patients, urinary calcium excretion was frequently much higher in the out-patient specimens. Third, our patients are much less highly selected than those studied in most stone clinics. With the kind co-operation of Dr Andrew Bruce and his urological colleagues, a large proportion of all stone patients in the region including many who have had only 1 or 2 stones (approximately one-third of our patients have had only 1 stone), have been referred for investigation. Thus, the stone patients which we have been studying should be roughly equivalent to those encountered in the average practice of urology.

The diagnoses made in the first 300 patients studied in Kingston are given in Table I. The notable features are (1) the relatively high incidence of hypercalciuria; (2) the diminishing incidence of struvite stones due to urinary tract infection; (3) an incidence of primary hyperparathyroidism of 2% which is considerably lower than that found in most stone clinics where patients are more highly selected (including our previous experience in Toronto where the incidence of primary hyperparathyroidism was 11%). Also of note is the fact that a diagnosis of medullary sponge kidney was made in only 5% of these patients. Shortly after this initial review was made, Dr Alan Rose informed us that in his experience the incidence of sponge kidneys in stone patients was considerably higher. Prompted by this observation, our examination of pyelograms for tubular ectasia has been much more assiduous in recent years so that in our last 100 diagnoses we have detected pyelographic evidence of this disorder in 25% of our patients. It should be emphasised that the radiographic changes seen in many patients are of minor degree and are not commented on by most radiologist or urologists. Minor degrees of tubular ectasia will escape detection if X-ray films do not outline the renal calyceal pattern with a high degree of clarity. In many stone patients the only pyelograms available are taken during an episode of renal colic when 1 kidney may be partially or completely obstructed and detail in the other obscured by bowel contents; fairly marked degrees of tubular ectasia may not be detected in X-ray examinations done under these conditions. It is likely, therefore, that the incidence of minor degrees of tubular ectasia is even higher than our figures would suggest.

It remains to be proven of course that a minor degree of tubular ectasia is related to the

---

[1] Supported by Research Grant MT681 from the Medical Research Council of Canada.

Read at the 32nd Annual Meeting of the British Association of Urological Surgeons in London, June 1976.

Table I

Renal Calculi—Kingston (1968-1976, 800 Cases)

	First 300 cases (%)		Last 100 cases (%)	
Calcium oxalate and/or phosphate		79		90
Normocalciuric (no systemic disease)	32		20	
Idiopathic hypercalciuria	34		33	
Medullary sponge kidney	5		25 (+7 suspect)	
Hyperparathyroidism	2		3	
Other	6		3	
Struvite (infection)		5		1
Uric acid		5		2
Cystine		1		1
Stone type uncertain		10		6

pathogenesis of stones. However, it would seem foolhardy to dismiss these changes as being of no significance and we must at least consider the possibility that many patients whom we now label as having idiopathic hypercalciuria or idiopathic calcium stones are not idiopathic at all but have a structural and functional abnormality of the nephron which predisposes to stone formation.

In view of the difficulty in obtaining pyelographic evidence of minor degrees of tubular ectasia, the need to establish other clinical, biochemical or genetic markers for this disorder becomes obvious. We have been impressed by the strong family history of stones in many of our patients. Perhaps the most striking example which we have encountered to date is the patient illustrated in Figure 1, where mother, 7 siblings and 3 nieces and nephews all had kidney stones.

Some years ago we drew attention to the fact that idiopathic hypercalciuria in the female was a distinctly uncommon condition and that the finding of sustained hypercalciuria in the female warrants a careful search for an underlying disorder such as hyperparathyroidism (Yendt and Gagne, 1968). With our increased awareness of the high incidence of sponge kidney, we are more reluctant than ever to diagnose idiopathic hypercalciuria in the female which we now believe is present in no more than 5% of all female stone patients; in other words, primary hyperparathyroidism occurs just as frequently as idiopathic hypercalciuria in female stone patients and sponge kidneys is much commoner than both these conditions. It is necessary at this point to define hypercalciuria. Although in the past we have adhered to the widely accepted upper limit of normal urinary calcium excretion as being 300 mg/24 hours in males and 250 mg/24 hours in females who are eating unrestricted diets, we have found, as have many others, that the upper limit of the 95% range in normal subjects studied under these conditions is somewhat higher (375 mg in males and 325 mg in females). For the purpose of this discussion we have defined hypercalciuria in the female as being urinary calcium excretion in excess of 325 mg/24 hours.

The pathogenesis of calcium stones is still a matter of considerable controversy but a brief summary of the current status of research on this subject is a useful prelude to a discussion on prevention. On the basis of our own work, we have concluded that the urine of patients with so-called "idiopathic" stones is normal with respect to volume, and the content of known inhibitors such as citrate, magnesium sodium and zinc. On the basis of most reports in the literature the same might be said for pyrophosphate although Fleisch (1976) has recently suggested that urine pyrophosphate is significantly reduced in male patients with calcium stones. The high incidence of hypercalciuria is of course well known; however, only recently has it become apparent that the oxalate content of the urine of the patient with calcium stones is significantly higher than in

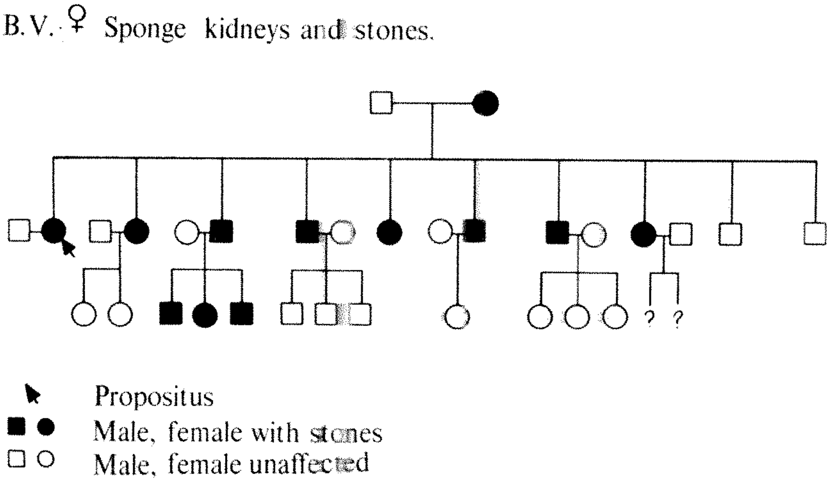

B.V. ♀ Sponge kidneys and stones.
? ?
Propositus
■ ● Male, female with stones
□ ○ Male, female unaffected

Fig. 1. Family tree of patient with renal calculi due to medullary sponge kidneys. The mother, 7 siblings and 3 nieces and nephews of the patient have all had kidney stones.

normal range. Thus it is not surprising that Robertson, Peacock and Nordin (1971) have found that the urine of patients with recurrent calcium oxalate is super-saturated with calcium oxalate to a greater degree (such that the formation product of calcium oxalate is frequently exceeded) than is the case with normal subjects. These same workers have also found that the stone patients excrete larger crystals of calcium oxalate in the urine than do normal subjects and they have concluded that there are inhibitors of calcium oxalate crystal growth in normal urine which is deficient in their patients. Dent and Sutor (1971) have reached similar conclusions. Other abnormalities of the urine of stone patients include the frequent presence of mucoprotein substance A which is also a constituent of the organic matrix of stones (Boyce, 1969) and a deficiency of an inhibitor of calcification of an organic matrix (Howard and Thomas, 1958) which is as yet unidentified (Barker *et al.*, 1974).

A host of remedies has been advocated for the prevention of calcium stones. Measures currently employed include increased fluid intake, reduction of dietary calcium and/or oxalate, restriction of dietary sodium chloride and the administration of various agents such as thiazides, orthophosphates, magnesium, cellulose phosphate, allopurinol, and diphosphonates. It is difficult to assess the value of many of these measures on the basis of published reports which tend to be inadequate in terms of patient numbers, duration of treatment and the provision of historical detail for individual patients in the pretreatment and post-treatment periods. However, our experience with thiazides is now of sufficient size (well over 300 patients) and duration (14 years) to justify the conclusion that these agents are highly effective and useful in the prevention of calcium stones. We believe that the reported experience with the use of orthophosphate particularly that of Howard and Thomas (1968), Thomas (1972) and Smith, Thomas and Arnaud (1973) allow the same conclusion to be drawn for that agent. It is more difficult to assess the efficacy of the other agents on the basis of reports published to date.

Before describing the effects of thiazides and orthophosphates in greater detail it is relevant to comment on the role of fluid intake and diet in the management of the patient with calcium stone. Most of us advise our patients to increase their fluid intake sufficiently to maintain a high urine volume—about 2 litres per day—and to drink sufficient fluids in the evening to prevent the urine from becoming too concentrated during the night. Such good advice is surprisingly hard to follow and many patients do not effectively maintain a high urine volume despite repeated

Table II

Oxalate in Juices + Beverages (Thomas, 1976)

	Oxalate (mg/l)		Oxalate (mg/l)
Fruit juices		Iced tea	68
Grapefruit	108	Instant tea	36
Orange	80	Beer (US)	17
Cranberry	66	Coffee	7
Grape	58	Coca Cola	5
Apple	11		

urgings to do so. Many patients dislike water and ask what other fluids are permissible: some recent data of Thomas on the oxalate content of fruit juices and beverages are of interest (Table II). It would seem reasonable to avoid an excessively high intake of certain fruit juices and tea because of their high oxalate content. Thomas (1976) has observed that urinary oxalate excretion may increase by approximately 50% following the ingestion of 2 quarts of tea per day and he has also noted that the ingestion of 1 quart of orange juice per day may increase the daily excretion of oxalate by as much as 40 mg in stone patients, but to a much lesser extent in normal subjects.

Restriction of dietary calcium has been widely advocated for the prevention of calcium stones. However, it has been our practice not to restrict dietary calcium except to correct obvious excesses. In our experience, restriction of dietary calcium was frequently ineffective in altering the cause of stone disease. In one of the few published reports on the efficacy of this measure Nordin *et al.* (1973) found that stone formation did not cease in two-thirds of 37 patients after institution of a low calcium diet. Moreover, we have been concerned about the possible adverse effects of long-term calcium restriction on the skeleton. Although the restriction of dairy products may significantly reduce urinary calcium, it is likely to lead also to reduced phosphate intake which in turn may diminish the excretion of pyrophosphate in the urine. It has also been shown that absorption of dietary oxalate is reduced in the presence of free calcium in the intestinal lumen and that reduced calcium intakes lead to increased excretion of oxalate in the urine. This suggests diets restricted in calcium are unlikely to be beneficial unless dietary oxalate is also restricted. A diet which is low in both calcium and oxalate content is extremely restrictive and unlikely to gain wide acceptability.

The direct relationship between urinary sodium and urinary calcium excretion is well established and there would appear to be a theoretical rationale for the restriction of dietary sodium chloride in patients with calcium stones. In practice, however, there are marked individual variations in this relationship and for this reason we doubt the wisdom of restricting dietary sodium chloride in stone patients on a routine basis. However, the hypercalciuric patient should probably be advised to reduce his salt intake to normal if it is obviously excessive.

As previously mentioned, the administration of orthophosphate has been shown to be an effective and useful measure in the prevention of calcium stones. However, the minimal effective dose must be sufficient to provide at least 1·5 g phosphorus per day which is given in 3 divided doses and in certain instances as much as 2·5 g per day may be necessary. When doses of this magnitude are employed, stone prevention is reported to cease in approximately 90% of patients treated but the success rate is much lower when smaller doses are employed (Ettinger and Kolb, 1973). Orthophosphate administration leads to reduced urinary calcium excretion and increased pyrophosphate excretion but it is still uncertain if these effects are sufficient to account entirely for its efficacy in stone prevention. The only immediate side-effects of phosphate administration are gastric upset and diarrhoea which will occasionally require discontinuation of treatment. Concern has been expressed that long continued administration of orthophosphates may adversely affect the skeleton by inducing secondary hyperparathyroidism which leads to an increased rate of bone resorption, but at the moment sufficient data are not available to assess the magnitude of this potential hazard.

Our experience with the use of hydrochlorothiazide in the prevention of calcium stones now spans a period of 14 years and includes well over 300 patients. In 1972 we completed a survey of our first 10 years' experience with this agent (Yendt and Cohanim, 1973). This was a survey of every patient in whom we had initiated thiazide prophylaxis for stones. There were 197 such patients at that time and the total number of patient years of treatment was well in excess of 700. We were able to obtain adequate follow-up data in all but 19 of these patients.. In another 39 patients hydrochlorothiazide was discontinued for a variety of reasons (but not because of therapeutic failure except in 2 patients in whom the drug was discontinued after a few days because no significant hypocalciuric effect was obtained); in 20 of these 39 patients, hydrochlorothiazide was discontinued because of side-effects attributable to the use of the drug. There remained 139 patients who have continued on treatment and who were adequately followed. Stone progression (*i.e.* formation of new stones or growth of stones present when therapy was initiated) has occurred in only 8 patients with non-infected calcium stones who have adhered to the regimen. Even these 8 patients are greatly improved over their pre-treatment status. There are an additional 7 patients in whom stone formation was arrested during thiazide therapy, but whose condition progressed after they had stopped thiazides or failed to take the full recommended dose. These patients have subsequently resumed taking the full dose of medication.

Although our initial use of hydrochlorothiazide was based on its hypocalciuric action, there are other effects which may be of equal or greater importance in stone prevention. There is a sustained increase in the urinary excretion of magnesium and zinc (Yendt, Gagne and Cohanim, 1966; Cohanim and Yendt, 1975). Both magnesium and zinc inhibit the calcification of an organic matrix *in vitro* (Mukai and Howard, 1963; Bird and Thomas, 1963) and magnesium also enhances the solubility of calcium oxalate in simple solutions (Desmars and Tawashi, 1973). Of perhaps even greater importance is the possibility that thiazides might reduce the urinary excretion of oxalates. Although we have been unable to demonstrate such an effect in short-term acute experiments, we have found that the mean urine oxalate was significantly lower in 37 patients studied before and during long-term thiazide therapy (urine oxalate excretion: pre-thiazides 32·3 ± 18·5 mg/24 hours, during thiazides 20·5 ± 14·7 mg/24 hours, P 0·01). In this study, urine oxalate was measured by the method of Archer *et al.* (1957). At the present time we are attempting to confirm these observations with newer and more accurate methodology. Such confirmation, if forthcoming, would provide us with a much more satisfactory explanation for the efficacy of thiazides in stone prevention and would place thiazides in the unique position as being the only agent which reduces the urinary excretion of both components of calcium oxalate stones. It may also provide us with an explanation for the following clinical observations (*a*) that stone formation may cease in some thiazide treated patients despite the fact that there has been little if any hypocalciuric effect of the drug; (*b*) in patients with extreme hypercalciuria, thiazides are usually effective despite the fact that the hypercalciuria may be only partially corrected.

It should be emphasised that the thiazide diuretics and related agents such as chlorthalidone and metolazone are the only diuretics which lower urine calcium excretion and are useful in stone prevention. Other diuretic agents such as furosemide and ethacrynic acid actually increase urine calcium and may aggravate stone formation.

Concerning the use of the thiazide diuretics, we do not restrict dietary calcium or sodium chloride except to correct excesses. Potassium supplements are not given routinely but all patients are provided with an instruction sheet outlining the effects of the drug on potassium metabolism which includes advice to increase the intake of high potassium foods and the warning that hypokalaemia should be corrected under the following circumstances: (i) coronary artery disease,

(ii) the administration of digitalis or a general anaesthetic or (iii) if the serum potassium falls below 3·0 mE/l. To minimise the incidence and severity of side-effects, we prefer to begin treatment with 25 mg hydrochlorothiazide per day and to increase the daily dose by 25 mg at weekly intervals until the maintenance dose of 50 mg twice daily is achieved. We do not restrict the use of this agent to patients with idiopathic hypercalciuria. It seems to be just as effective in normocalciuric patients with stones and in patients with medullary sponge kidneys. When considering the possible use of a thiazide diuretic, there is no need to differentiate the so-called absorptive and renal hypercalciurics and we have made no attempt to do so in our practice.

Faced with a patient with recurrent calcium stones who is in obvious need of an effective prophylactic regimen, which regimen should be prescribed, orthophosphates or a thiazide? If the patient is also hypertensive, an association which occurs frequently in our experience, the choice is easy because thiazides are excellent treatment for both conditions. Moreover, if there is any suspicion of primary hyperparathyroidism, thiazide is again the drug of choice because this agent may sometimes (but not always) unmask the condition by causing sustained hypercalcaemia (Yendt, Guay and Garcia, 1970), whereas, phosphate administration may reduce serum calcium levels in hyperparathyroidism. On the other hand, associated gout or diabetes may favour the use of orthophosphates. In this regard, however, it should be emphasised that gout and diabetes are not absolute contra-indications to the use of a thiazide for stone prevention. We are treating a number of gouty patients effectively with both hydrochlorothiazide and allopurinol and have demonstrated that the associated use of allopurinol does not alter the effects of hydrochlorothiazide on urinary calcium and magnesium excretion (Yendt, 1970). Furthermore, the administration of a thiazide is not likely to aggravate the severity of diabetes if thiazide-induced hypokalaemia is corrected. In the absence of any of these associated conditions, the choice between orthophosphates and thiazides is at the moment largely a matter of personal preference. One must balance the convenience and low cost of a thiazide against the probability of fewer immediate side effects with orthophosphates.

Encouraging results have also been reported with the administration of allopurinol for the prevention of calcium stones (Coe and Kavalach, 1974). The rationale for the use of this agent is the frequent finding of hyperuricosuria in many calcium stone patients and the possibility that crystals of sodium urate and uric acid could promote epitaxial growth of calcium oxalate crystals; it remains to be demonstrated that the urine of these patients is sufficiently saturated with sodium urate to give spontaneous crystal formation *i.e.* that the formation product for sodium urate is exceeded. It is still too early to make a final assessment of the role of allopurinol in stone prevention but because of its relative freedom from side-effects further study is obviously warranted.

Cellulose phosphate in conjunction with a low calcium diet has been reported to correct absorptive hypercalciuria and to prevent stone formation in a small number of stone patients associated with this disorder (Pak, Delea and Bartter, 1973). However, this agent is unlikely to become a popular mode of therapy because it is expensive, bulky and must be taken with meals in a dose of 15-30 g per day. Its use should probably be restricted to patients with absorptive hypercalciuria. There is danger of magnesium deficiency unless magnesium supplements are provided as well.

The administration of magnesium oxide has also been reported to reduce stone formation in patients with recurrent calcium oxalate stones (Melnick *et al.*, 1971; Prien, personal communication, 1972), although it would appear that this agent is considerably less effective than thiazides or orthophosphate. Despite this, however, the use of magnesium warrants further trials because it is cheap, convenient and free of side-effects other than diarrhoea. Moreover, unlike most other agents, it can safely be prescribed on a long-term basis without the need for a regular medical supervision. It may be useful in the management of the patient with less frequent stone recurrences or in patients who are reluctant to embark on a more effective regimen.

The efficacy of diphosphonate, an agent which inhibits the nucleation and crystal growth of calcium oxalate (Pak, Ohata and Holt, 1975), is presently being assessed in a double-blind multicentre clinical trial in the USA. The results of this trial are as yet unknown but it is unlikely that this compound will prove to be suitable for widespread use in view of its adverse effects on the skeleton when administered on a long-term basis.

Summary

Results of investigation of 800 patients with renal calculi are presented.

The high incidence of medullary sponge kidneys (tubular ectasia) in patients of either sex is stressed as is the low incidence of idiopathic hypercalciuria in the female.

Hydrochlorothiazide has been found to be highly effective in preventing recurrence of calcium stones in our personal experience with over 300 patients who have been treated for as long as 14 years with this agent.

The efficacy and mode of action of other measures advocated for stone prevention is reviewed.

References

ARCHER, H. E., DORMER, A. E., SCOWEN, E. F. and WATTS, R. W. E. (1957). Studies on the urinary excretion of oxalate by normal subjects. *Clinical Science*, **16**, 405-411.

BARKER, L. M., PALLANTE, S. L., EISENBERG, H., JOULE, J. A., BECKER, G. L. and HOWARD, J. E. (1974). Simple synthetic and natural urines have equivalent anticalcifying properties. *Investigative Urology*, **12**, 79-81.

BIRD, E. D. and THOMAS, W. C., (1963). Effects of various metals on mineralization *in vitro*. *Proceedings of the Society for Experimental Biology and Medicine*, **112**, 640-643.

BOYCE, W. H. (1969). Organic matrix of native human urinary concretions. In *Renal Stone Research Symposium*, ed. A. Hodgkinson and B. E. C. Nordin. London: Churchill, pp. 93-104.

COE, F. L. and KAVALACH, A. G. (1974). Hypercalciuria and hyperuricosuria in patients with calcium nephrolithiasis. *New England Journal of Medicine*, **291**, 1344-1350.

COHANIM, M. and YENDT, E. R. (1975). The effects of thiazides on serum and urinary zinc in patients with renal calculi. *Johns Hopkins Medical Journal*, **136**, 137-141.

DENT, C. E. and SUTOR, D. J. (1971). Presence or absence of inhibitor of calcium-oxalate crystal growth in urine of normals and of stone formers. *Lancet*, **2**, 775-778.

DESMARS, J. F. and TAWASHI, R. (1973). Dissolution and growth of calcium oxalate monohydrate. I. Effect of magnesium and pH. *Biochimica et Biophysica Acta*, **313**, 256-267.

ETTINGER, B., and KOLB, F. O. (1973). Inorganic phosphate treatment of nephrolithiasis. *American Journal of Medicine*, **55**, 32-37.

FLEISCH, H. (1976). The inhibitor concept of stone formation. Presented to the International Symposium on Idiopathic Urinary Bladder Stone Disease. Bethesda, Maryland, April 20-23, 1976.

HOWARD, J. E. and THOMAS, W. C., JR. (1968). Control of crystallization in urine. *American Journal of Medicine*, **45**, 693-699.

MELNICK, I., LANDES, R. R., HOFFMAN, A. A. and BURCH, J. F. (1971). Magnesium therapy for recurring calcium oxalate urinary calculi. *Journal of Urology*, **105**, 119-122.

MUKAI, T. and HOWARD, J. E. (1963). Some observations on the calcification of rachitic rat cartilage by urine. *Bulletin of the Johns Hopkins Hospital*, **112**, 279-290.

NORDIN, B. E. C., BARRY, H., BULUSU, L. and SPEED, R. (1973). Dietary treatment of recurrent calcium stones disease. In *Urinary Calculi. Proceedings of the Int. Symp. Renal Stone Res., Madrid, 1972*, ed. L. Cifuente Delatte and others. Basel: Karger, pp. 170-176.

PAK, C. Y. C., DELEA, C. S. and BARTTER, F. C. (1974). Successful treatment of recurrent nephrolithiasis (calcium stones) with cellulose phosphate. *New England Journal of Medicine*, **290**, 175-180.

PAK, C. Y. C., OHATA, M. and HOLT, K. (1975). Effect of diphosphonate on crystallization of calcium oxalate *in vitro*. *Kidney International*, **7**, 154-160.

ROBERTSON, W. G., PEACOCK, M. and NORDIN, B. E. C. (1971). Calcium oxalate crystalluria and urine saturation in recurrent renal stone-formers. *Clinical Science*, **40**, 365-374.

SMITH, L. H., THOMAS, W. C. and ARNAUD, C. D. (1973). Orthophosphate therapy in calcium renal lithiasis. In *Urinary Calculi. Proceedings of the Int. Symp. Renal Stone Res., Madrid, 1972.* Karger, Basel: pp. 188-197.

THOMAS, W. C. (1972). Effectiveness and mode of action of orthophosphates in patients with calcareous renal calculi. *Transactions of the American Clinical and Climatological Association*, **83**, 113-124.

THOMAS, W. C. (1976). Dietary factors in urinary crystal formation. Presented to the International Symposium on Idiopathic Urinary Bladder Stone Disease. Bethesda, Maryland, U.S.A., April 20-23, 1976.

YENDT, E. R. (1970). Renal calculi. *Canadian Medical Association Journal*, **102**, 479-489.

Yendt, E. R. and Cohanim, M. (1973). Ten years' experience with the use of thiazide in the prevention of kidney stones. *Transactions of the American Clinical and Climatological Association*, **85**, 65-75.

Yendt, E. R. and Gagne, R. J. A. (1968). Detection of primary hyperparathyroidism, with special reference to its occurrence in hypercalciuric females with "normal" or borderline serum calcium. *Canadian Medical Association Journal*, **98**, 331-336.

Yendt, E. R., Gagne, R. J. A. and Cohanim, M. (1966). The effects of thiazides in idiopathic hypercalciuria. *American Journal of Medical Science*, **251**, 449-460.

Yendt, E. R., Guay, G. F. and Garcia, D. A. (1970). The use of thiazides in the prevention of renal calculi. *Canadian Medical Association Journal*, **102**, 614-620.

The Authors

E. R. Yendt, MD, FRCP(C), Professor.
M. Cohanim, MD, Associate Professor.

British Journal of Urology (1976), **48**, 515-524 ©

Crystalluria in Normal Subjects and in Stone Formers With and Without Thiazide and Cellulose Phosphate Treatment

P. C. HALLSON and G. ALAN ROSE
St Peter's Hospitals and Institute of Urology, London

Idiopathic hypercalciuria is the commonest cause of renal calculi in this country (Rose and Harrison, 1974) and also in some overseas countries where studies have been published (Yendt, 1970; Revusova, Zvara and Gratzlova, 1973).

Because it is known that the long-term recurrence rate for renal calculi is high (Williams, 1963) it has generally been agreed desirable to lower urinary calcium in those calcium rich stone formers who show hypercalciuria. Apart from simple restriction of the calcium rich foods (milk, cheese and their products) 3 distinct drug therapies are now available, namely inorganic phosphates, thiazide diuretics and cellulose phosphate. The latter 2 therapies have been used extensively in these hospitals for a period of over 10 years but although we have a clinical impression of benefit, it has been impossible so far to prove that these therapies are in fact effective in reducing the recurrence rate for renal calculi.

An alternative approach to the question of whether treatment is effective is to study the chemical composition of urine. However, the changes produced in urine composition by the drugs used to lower urinary calcium are rather complex. For example, it has been shown that cellulose phosphate dramatically raises urinary oxalate (Marshall and Barry, 1973; Hallson, Kasidas and Rose, 1977) and lowers urinary magnesium (Dent, Harper and Parfitt, 1964; Teotia *et al.*, 1974) while thiazides have been shown to lower urinary citrate (Garcia and Yendt, 1970). It is therefore difficult to know whether the treatments used in fact lead to an increase or decrease in saturation of urine with regard to calcium oxalate and phosphate. Valiant attempts have been made (Robertson, Peacock and Nordin, 1968) to measure calcium and oxalate or phosphate ion activity products in urine but unfortunately the methods on which these calculations are based are not sufficiently accurate and are open to errors. For example, although it is essential in these calculations to know ionic strength, there is no way to measure this, and to find it out one has to add up all the ionic strengths of all the components, a formidable and well-nigh impossible task in a solution as complex as urine. Since ionic strength of a particular ion is dependent upon the square of the ionic charge, certain di- and tri-valent organic acids not brought into the calculation assume considerable importance and their omission leads to corresponding errors.

Fortunately, a neater approach was suggested by the work of Dyer and Nordin (1967) and Robertson, Peacock and Nordin (1971) when they studied and measured crystals of calcium oxalate in urine. There can be no escape from the conclusion that the presence of crystals proves super-saturation. However, Robertson *et al.* (1971) only studied 6 patients and the studies were carried out in a metabolic ward in carefully regulated conditions. It was therefore thought of

Read at the 32nd Annual Meeting of the British Association of Urological Surgeons in London, June 1976.

interest to study crystals in the urine of normal subjects and patients undergoing treatment for idiopathic hypercalciuria while under home conditions of diet and activity.

Methods

The subjects studied were all adults and either normal volunteers or stone formers in whom a diagnosis of idiopathic hypercalciuria had been made and who were either untreated or receiving treatment with thiazide diuretics (usually bendrofluazide 5-10 mg per 24 hours and/or cellulose phosphate 10-30 g per 24 hours). Some of these patients were previously described in the series of Rose and Harrison (1974) but many new cases have since been added using the same criteria of diagnosis.

Specimens of urine were either random samples or collected in an overnight procedure. The random samples were all in fact obtained at 10 a.m.-12 noon, the period during which the metabolic stone clinic takes place. There was no patient preparation and indeed patients were deliberately not warned that a special test was to take place. In the overnight test patients were given written instructions on the procedure. They were told to carry on as normal until the morning of the test when they should pass their early morning urine (EMU1) into the thermos flask provided. They should then have a dry breakfast, bring the thermos flask to the hospital and pass the second urine (EMU2) into the second thermos flask. It was hoped that the random and EMU1 samples would correspond to the normal situation for each patient while EMU2 would reveal the effects of mild dehydration. Each urine was studied as soon as possible and always within 1 to 2 hours of receipt in the laboratory. All subsequent studies were carried out at 37°C. Each urine was subjected to crystal counting by Coulter Counter as described by Robertson (1969) and the nature of the crystals was revealed by light microscopy on a warmed stage observing the deposit obtained after centrifugation of the urine at 37°C. When appropriate the effects of acetic and hydrochloric acids upon the crystals were observed in order to help establish their chemical nature. Any sample showing signs of infection was rejected from the study. Urinary pH was measured with a glass electrode and meter.

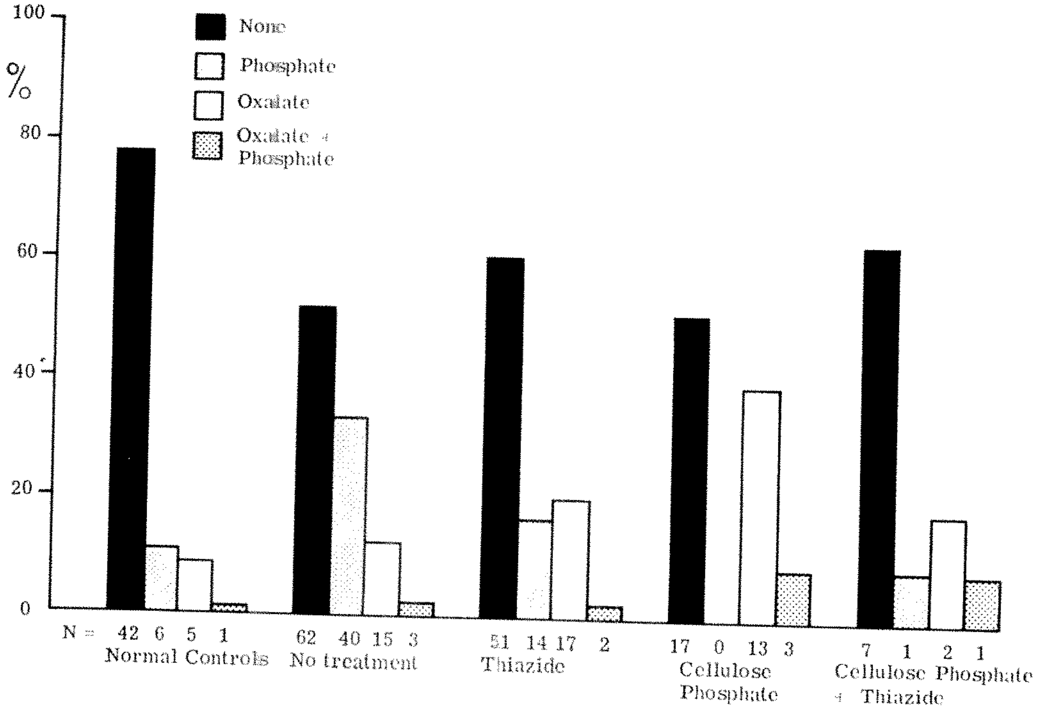


Fig. 1. Incidence of phosphate and oxalate crystals in all urine samples from normal subjects and stone formers untreated and on treatment with thiazides and/or cellulose phosphate.

Results and Discussion

The results obtained can be considered in various ways according to the criteria used. Thus one may consider the effect of treatment upon incidence of urine samples showing crystals, or the type of crystals occurring, or the crystal volume concentrations occurring, and finally the degree of aggregation of crystals. We can not know in advance which of these criteria has most significance with regard to incidence of stone formation and it is therefore necessary to study each of these factors separately.

1. *Incidence of Crystals*

Figures for the incidence of the various crystal types are shown in Figure 1. It is seen that some 78% of the samples of urine from normal individuals were crystal-free and that samples showing either phosphate or oxalate crystals occurred in approximately equal numbers. In the case of untreated stone formers, however, only 52% of the samples were crystal-free and when crystals were present they were most frequently calcium phosphate. Thus 33% of stone formers showed phosphate crystals compared with only 11% for normal subjects, and 12% of the stone formers showed oxalate crystals compared with 9% of the normal subjects. The main difference between normal subjects and stone formers therefore appears to be the increased incidence of phosphate crystals in the latter. Treatment with thiazide considerably reduces the incidence of phosphate crystals but slightly increases the incidence of oxalate crystals from 13 to 20%, leaving an increase in the crystal-free samples to 60%. The results of cellulose phosphate therapy are quite remarkable showing a nearly complete disappearance of phosphate crystals but a striking increase in incidence of oxalate crystals to 40% so that the incidence of crystal-free samples is virtually unchanged by the treatment. The treatment most effective in reducing crystal incidence as a whole was the combination of cellulose phosphate and thiazide.

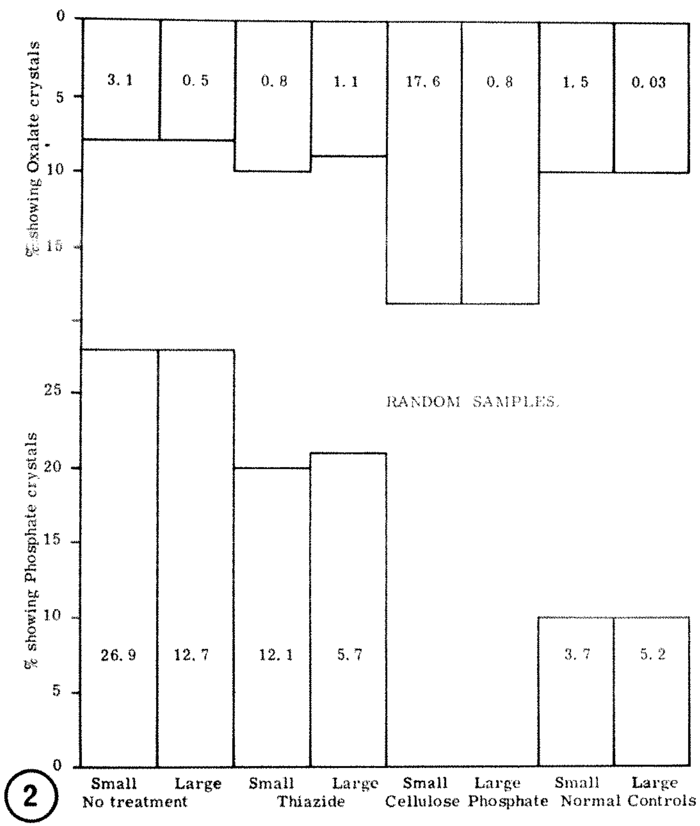
2. *Volume and Size of Crystals*

In Figures 2 and 3, the data shown in Figure 1 have been subdivided so as to distinguish urine samples with small crystals from those with large crystals. The dividing line for this purpose has been taken as 12 μ because it was reported by Robertson and Peacock (1972) that urinary crystals showed a bi-modal distribution with regard to volume with a dividing line of 12 μ. Our own results agree in the main with these findings although there were striking exceptions. Figure 2 shows that in the random samples of urine of stone formers, both small and large phosphate crystals occurred more frequently and in greater volume than in samples from normal subjects. However oxalate crystals, although occurring with similar incidence in stone formers and normal subjects, showed larger volumes in the former. In particular we agree with Robertson and Peacock (1972) that the large oxalate crystals occur in very much smaller volume concentrations in normal subjects than in stone formers. Thiazide led to a fall in both incidence and volume of large and small phosphate crystals, but a rise in volume of large oxalate crystals. Cellulose phosphate led to a disappearance of all phosphate crystals but the incidence of small and large oxalate crystals increased dramatically as did the volume of small oxalate crystals.

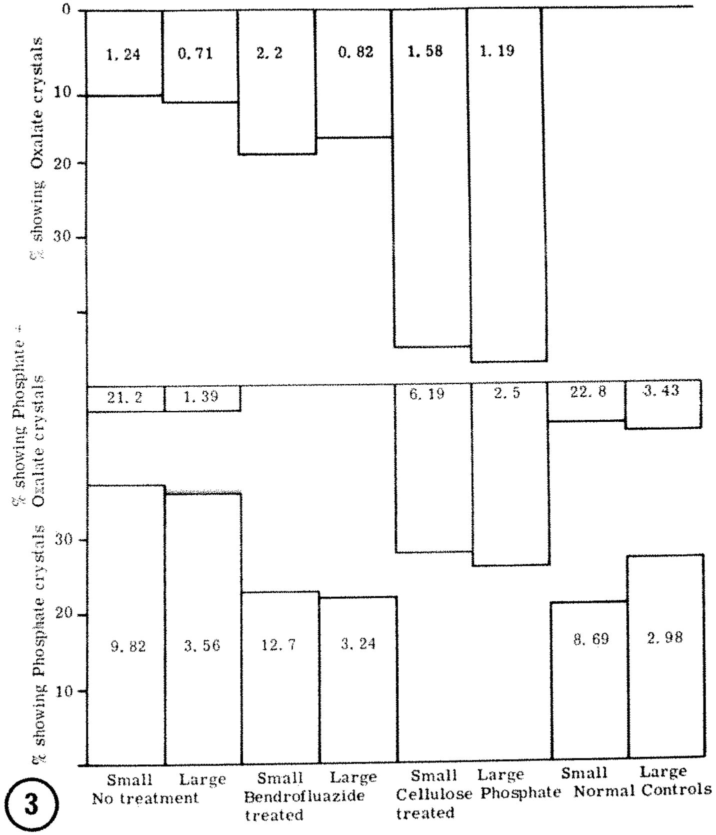
Figure 3 shows corresponding results for the early morning urine samples. The general trends seem similar to those for Figure 2 but they are not as easy to interpret because of the occurrence of mixtures of phosphate and oxalate crystals in the same urine samples.

3. *Crystal Volume Concentrations*

In order to compare crystal volume concentrations in urine samples, they have been divided up into those with none to small, medium-sized and large crystals volume concentrations and



2



3

Fig. 2. Effect of treatment upon crystal volume and incidence. Data from Figure 1 restricted to random urine samples, but subdivided into crystals below 12 μ (small) and those above 12 μ (large) in diameter. The numbers in the columns indicate mean crystal volume concentrations within their particular columns.

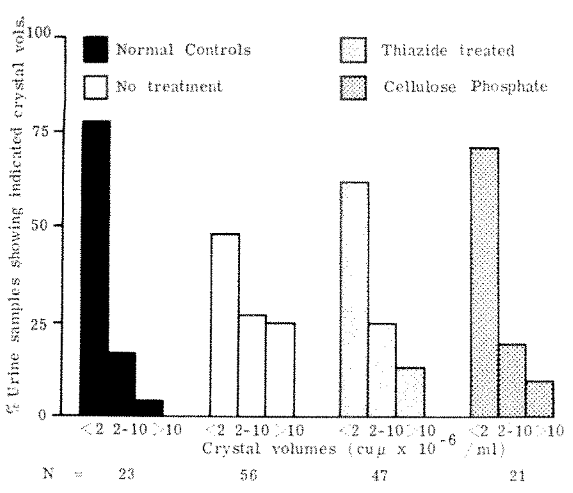
Fig. 3. Effect of treatment upon crystal volume and incidence. Data from Figure 1 restricted to early morning urines (EMU 1 and 2) and subdivided into crystals below 12 μ (small) and those above 12 μ (large) in diameter. The numbers within the columns indicate mean crystal volume concentrations within their particular columns.

the results presented in Figures 4 and 5. When random urine samples are studied (Fig. 4) the results are clear-cut showing that untreated patients have about a 5-fold increase in the incidence of high crystal volume concentration and this incidence is halved either by thiazide or by cellulose phosphate. However, when the corresponding data are studied in the overnight EMU1 samples of urine (Fig. 5) the normal controls and stone formers are very similar to one another, while thiazide and cellulose phosphate appear to have very little effect. Results from EMU2 samples (Fig. 5) are somewhat different again with a considerable increase in large crystal volume concentrations in stone formers over normals and a reduction in these large volumes only by thiazide. These results are taken to mean that both thiazide and cellulose phosphate are shown to be beneficial in random urines and that the study of effect of treatment upon urine crystal volume concentrations on early morning urines is less helpful than the similar study on random urine samples.

4. *Aggregation of Calcium Oxalate Crystals*

Table I shows the incidence of aggregation of calcium oxalate crystals in various groups studied. It is seen that aggregation occurred only in 2% of the normal samples (in fact 1 out of 54) compared with an incidence of 8% (10 out of 121) in untreated stone formers. These results confirm the observation of Robertson, Peacock and Nordin (1969) that stone formers differ from normal subjects in that the former showed much more aggregation of octahedral calcium oxalate crystals than the latter. Table I also shows that treatment with thiazides resulted in a small increase, and cellulose phosphate in a much larger increase in the overall incidence of oxalate crystals (also shown above). Note, however, that the overall percentage of samples showing aggregation was virtually unchanged by these treatments. If it were to be conceded that

④



⑤

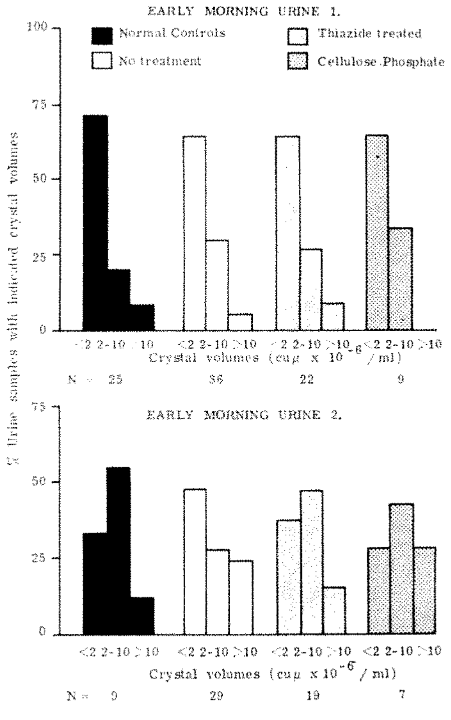


Fig. 4. Incidence of random urine samples showing 0-small, moderate and large crystal volume concentrations according to treatment.

Fig. 5. Incidence of early morning urine samples showing 0-small, moderate or large crystal volume concentrations according to treatment.

Table I

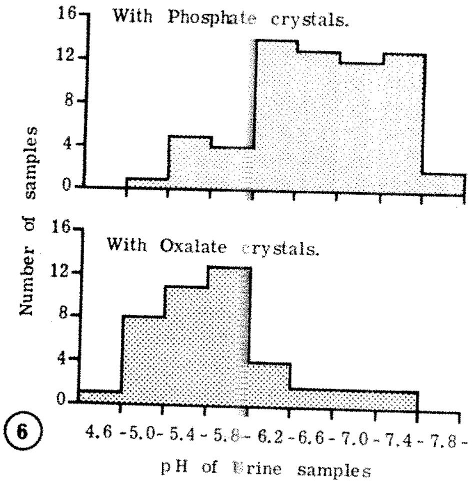
Incidence of Oxalate Crystal Aggregation in Oxalate (and Phosphate) Crystal Formers

	Normal subjects	Stone formers Untreated	Cellulose phosphate treated	Thiazide treated
No. without oxalate crystals	48	102	17	65
No. with oxalate crystals:				
(*a*) Without aggregation	5	9	14	13
(*b*) With aggregation	1	10	3	8
% with oxalate crystals	11	16	50	24
% of crystal formers showing aggregation	17	52	17	38
% of total samples showing aggregation	2	8	9	9

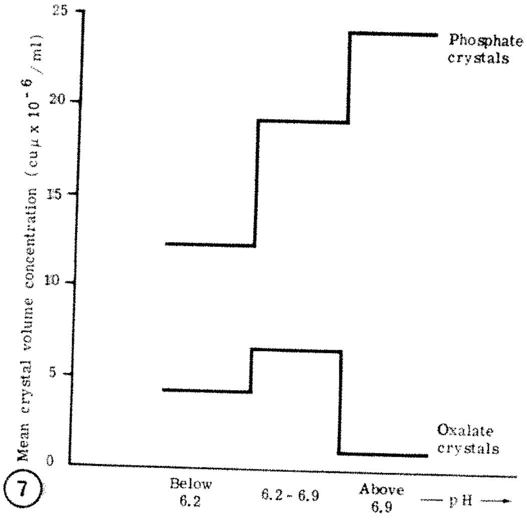
aggregation of oxalate crystals was an accurate indicator of the tendency of stone formation, then it would follow that this tendency is unchanged by use of thiazide or cellulose phosphate.

Urinary pH and Relation to Treatment of Crystal Type

It remains to be considered whether the changes in crystalluria resulting from treatment could be secondary to changes in urinary pH. Figures 6 and 7 show that urine pH determines both the relative incidence and crystal volume concentrations of calcium oxalate and phosphate respectively. Thus when urine pH is above 6·2 any crystals present are likely to be calcium phosphate, while below this pH they tend to be calcium oxalate. This finding confirms the work of Robertson *et al.* (1969). Therefore the possibility that changes from one crystal type to the other with treatment could be due to changes in the urine pH must be considered. Figure 8 shows that while normal subjects have a slightly lower urine pH than the stone formers, treatment



⑥



⑦

Fig. 6. Effect of urine pH upon incidence of urine samples showing oxalate and phosphate crystals respectively.

Fig. 7. Effects of urine pH upon mean crystal volume concentrations of phosphate and oxalate crystals respectively.

with thiazide or cellulose phosphate does not alter urine pH. It is therefore clear that the rather striking changes in crystal type brought about by thiazide and by cellulose phosphate cannot be explained by changes in urinary pH.

Previous work in the field of urinary crystals has been extremely confusing and conflicting. Dyer and Nordin (1967) seem to have been the first to point out that observations on urinary crystals are valueless unless performed on fresh specimens at 37°C. They observed that the only crystals found in warm and fresh samples of urine were octahedral calcium oxalate di-hydrate and amorphous calcium phosphate. They found these crystals in urine samples from both normal subjects and stone formers but gave no indication about the frequency of the findings. Robertson, Peacock and Nordin (1969) studied 6 males with recurrent idiopathic stone formation and 6 controlled subjects, all in a metabolic ward on controlled diet and fluid intake. They found that both groups showed both oxalate and phosphate crystals, but at any given urinary pH between 5 and 6·2 the stone formers showed the greater volume concentration of oxalate crystals and that this difference was explained by size of the crystals. Thus the controls showed small particles of 3 to 4 μ in diameter whereas the stone formers passed large octahedral crystals of 10 to 12 μ in diameter and often aggregated together in clumps of 20 to 300 μ diameter. In a later paper, however, the same authors (Robertson, Peacock and Nordin, 1971) studied similar patients in the same way and apparently found only oxalate crystals. In a brief communication Lemann

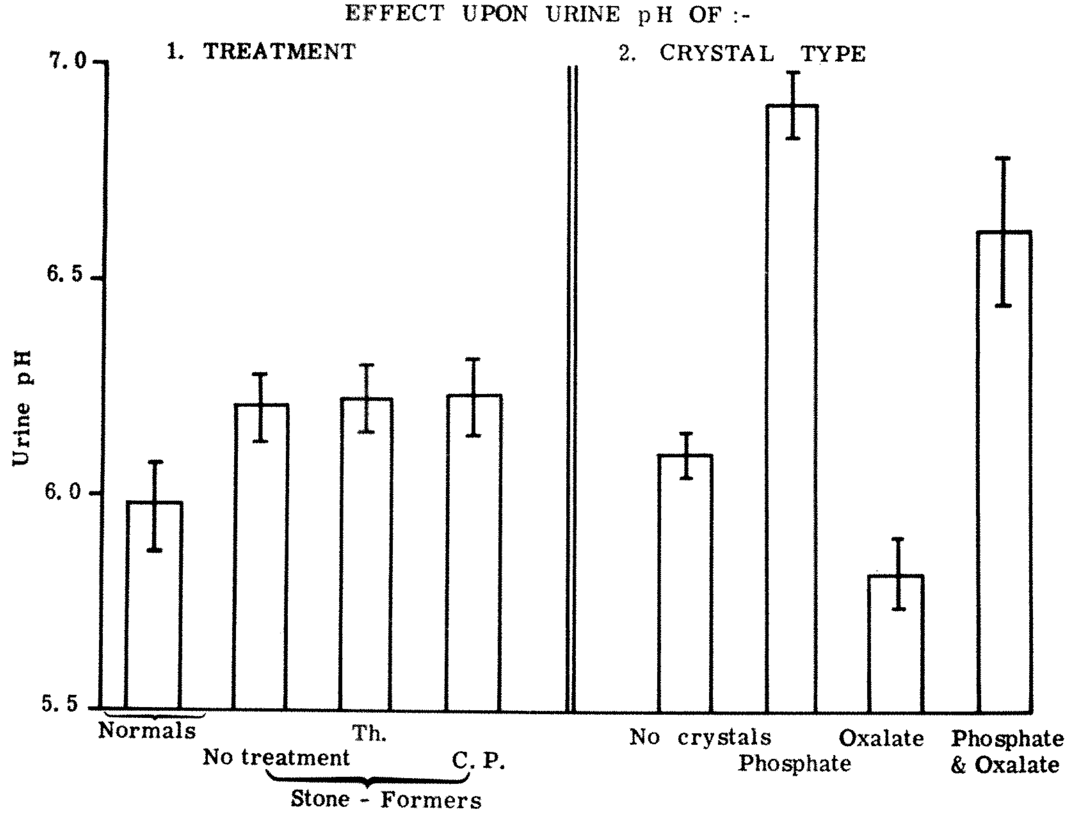


Fig. 8. Mean urinary pH (and SEM) of samples without and with oxalate and phosphate crystals and according to type of subject and treatment.

Table II

Ways in which Stone Formers Differ from Normal Subjects

1. Increased incidence of crystals, mainly due to phosphate.
2. Greater volume concentrations of both large and small phosphate and oxalate crystals.
3. Higher incidence of large crystal volumes.
4. Higher incidence of oxalate crystal aggregation.

Table III

Effects of Cellulose Phosphate upon Urinary Crystals

1. Incidence of:
    (*a*) Phosphate crystals greatly reduced.
    (*b*) Oxalate crystals greatly increased.
2. Small crystal volumes increased.
    Large crystal volumes unchanged.
3. Aggregation of oxalate crystals unchanged.

and Doner (1971) reported that after overnight thirsting there were no crystals in the urine samples of 15 normal subjects whereas calcium oxalate or phosphate crystals were present in samples from 10 out of 13 stone formers. The reason for these differences in findings are not clear but it should be noted that the conditions under which the patients have been studied were quite different in this study and those of Robertson *et al.* Here we have been observing patients under home conditions, whereas Robertson was observing them as in-patients in a controlled environment.

The therapeutic implications of the present work must now be considered. Although it does not seem possible to separate normal individuals from stone formers simply on the basis of occurrence, type or concentration of crystals present in random or overnight samples of urine as appeared to be the case from the work of Lemann and Doner (1971), certain differences have been observed and these are summarised in Table II. Possibly the most striking difference is the rarity of oxalate crystal aggregation in normal subjects compared to the stone formers. The effects of cellulose phosphate are summarised in Table III. The remarkable disappearance of phosphate crystals on treatment with cellulose phosphate is presumably a gain and in keeping with the studies which show a fall in calcium phosphate (Brushite) ion activity product with this treatment (Pak, Delea and Bartter, 1974). However, the same drug also produces a remarkable rise in oxalate crystals which is compatible with the rise in urinary oxalate induced by cellulose phosphate (see above) but not compatible with the reduction in calcium oxalate activity product observed by Hayashi, Kaplan and Pak (1975). Such a rise in oxalate crystalluria in patients whose stones are made predominantly of calcium oxalate seems at first sight a bad prognostic indicator. However, it may well be important that the increase in these crystals is confined to the small type and that they remain unaggregated so that they might not after all be a bad prognostic sign since such small oxalate crystals are seen not infrequently in normal subjects. The question of whether cellulose phosphate therapy is of benefit must therefore remain highly debatable and unanswered. It is of great theoretical interest that the large increase in oxalate crystals induced by cellulose phosphate is wholly attributable to a mass of small crystals which remain unaggregated (see Table I) and this lack of aggregation seems to require an explanation. Cellulose phosphate is known to cause a rise in urinary phosphate (Dent *et al.*, 1963) and a rise

Table IV

Effects of Thiazides upon Urinary Crystals

1. Incidence of:
    (*a*) Phosphate crystals greatly reduced.
    (*b*) Oxalate crystals marginally increased.
2. Large crystal volumes reduced.
3. Aggregation of oxalate crystals unchanged.

in urinary phosphate is known to cause a rise in urinary pyrophosphate (Russell and Hodgkinson, 1966) which, according to some authors, inhibits calcium oxalate crystal aggregation (Meyer and Smith, 1975). The effects of thiazides upon urinary crystals are summarised in Table IV. They appear distinctly encouraging in showing a reduction in phosphate crystals with only a minimal rise in oxalate crystals. This rise in oxalate crystals on thiazide treatment is not easy to explain and may indeed be not statistically significant. It is worth noting, however, that both Marshall and Barry (1973) and Hallson, Kasidas and Rose (1977) both noted a small but not statistically significant rise in urinary oxalate with thiazide treatment suggesting that this rise might in fact be real and be responsible for the similar rise in oxalate crystal incidence.

Summary

Quantitative and qualitative studies have been made of the urinary crystals from a series of normal subjects and from stone formers with idiopathic hypercalciuria with and without treatment with thiazide diuretics and/or cellulose phosphate.

The results obtained from mid-morning unprepared subjects seemed more helpful than those obtained following overnight collections or after a dry breakfast. Crystalluria was more common in stone formers than in normal subjects, but was seen in both groups. The most striking difference between these 2 groups was the almost complete absence of aggregation of oxalate crystals in the normal subjects.

Cellulose phosphate greatly reduced phosphate crystals but resulted in a large increase in small oxalate crystals but without change in the incidence of aggregation of oxalate crystals.

Thiazides also reduced occurrence of phosphate crystals but only gave a very small increase in oxalate crystals and also without change in aggregation of oxalate crystals.

The Coulter Counter was kindly donated by the Post-Graduate Medical Federation of the University of London. The work was financed by the St Peter's Research Trust.

We are also grateful to the normal volunteers for their co-operation in providing specimens and to Sister Kendrick for assisting with the collection of urine samples.

References

DENT, C. E., HARPER, C. M. and PARFITT, A. M. (1964). The effect of cellulose phosphate on calcium metabolism in patients with hypercalciuria. *Clinical Science*, **27**, 417-425.

DYER, R. and NORDIN, B. E. C. (1967). Urinary crystals and their relation to stone formation. *Nature*, **215**, 751-752.

GARCIA, D. A. and YENDT, E. R. (1970). The effects of probenecid and thiazides and their combination on the urinary excretion of electrolytes and on acid-base equilibrium. *Canadian Medical Association Journal*, **103**, 473-483.

HALLSON, P. C., KASIDAS, G. P. and ROSE, G. A. (1977). Urinary oxalate in summer and winter in normal subjects and in stone forming patients with idiopathic hypercalciuria, both untreated and treated with thiazide and/or cellulose phosphate. *Urological Research* (in press).

HAYASHI, Y., KAPLAN, R. A. and PAK, C. Y. C. (1975). Effect of sodium cellulose phosphate therapy on crystallization of calcium oxalate in urine. *Metabolism*, **24**, 1273-1278.

LEMANN, J. and DONOR, D. W. (1971). Calcium crystalluria. *Journal of Clinical Investigation*, **50**, 58a.

MARSHALL, R. W. and BARRY, H. (1973). Urine saturation and the formation of calcium-containing renal calculi: the effects of various forms of therapy. In *Urinary Calculi.* Proceedings of the International Symposium on Renal Stone Research, Madrid, 1972. Basel: Karger, pp. 164-169.

MEYER, J. L. and SMITH, L. H. (1975). Growth of calcium oxalate crystals. II. Inhibition by natural urinary crystal growth inhibitors. *Investigative Urology*, **13**, 36-39.

PAK, C. Y. C., DELEA, C. S. and BARTTER, F. C. (1974). Successful treatment of recurrent nephrolithiasis (calcium stones) with cellulose phosphate. *New England Journal of Medicine*, **290**, 175-180.

REVUSOVA, V., ZVARA, V. and GRATZLOVA, J. (1973). Urinary zinc secretion in patients with urolithiasis. *Urologia Internationalis*, **28**, 72-79.

ROBERTSON, W. G. (1969). A method for measuring calcium crystalluria. *Clinica Chimica Acta*, **26**, 105-110.

ROBERTSON, W. G. and PEACOCK, M. (1972). Calcium oxalate crystalluria and inhibitors of crystallization in recurrent renal stone-formers. *Clinical Science*, **43**, 499-506.

ROBERTSON, W. G., PEACOCK, M. and NORDIN, B. E. C. (1968). Activity products in stone-forming and non-stone-forming urine. *Clinical Science*, **34**, 579-594.

ROBERTSON, W. G., PEACOCK, M. and NORDIN, B. E. C. (1969). Calcium crystalluria in recurrent renal stone formers. *Lancet*, **2**, 21-24.

ROBERTSON, W. G., PEACOCK, M. and NORDIN, B. E. C. (1971). Calcium oxalate crystalluria and urine saturation in recurrent renal stone-formers. *Clinical Science*, **40**, 365-374.

ROSE, G. A. and HARRISON, A. R. (1974). The incidence, investigation and treatment of idopathic hypercalciuria. *British Journal of Urology*, **46**, 261-274.

RUSSELL, R. G. G. and HODGKINSON, A. (1966). The urinary secretion of inorganic pyrophosphate by normal subjects and patients with renal calculus. *Clinical Science*, **31**, 51-62.

TEOTIA, M., TEOTIA, S. P., SINGH, R. K. and TEOTIA, N. P. (1974). Treatment of idiopathic hypercalciuria and nephrolithiasis with sodium cellulose phosphate. *Journal of the Association of Physicians of India*, **22**, 709-714.

WILLIAMS, R. E. (1963). Long-term survey of 538 patients with upper urinary tract stone. *British Journal of Urology*, **35**, 416-437.

YENDT, R. E. (1970). Renal calculi. *Canadian Medical Association Journal*, **102**, 479-489.

The Authors

P. C. Hallson, MPhil, Research Biochemist, Institute of Urology.

G. Alan Rose, FRCP, MRCPath, FRIC, Consultant Chemical Pathologist, St Peter's Hospitals.

Requests for reprints to: Dr G. A. Rose, Department of Pathology, St Paul's Hospital, 24 Endell St., London WC2 9AE.

British Journal of Urology (1976), **48**, 525-530 ©

Size of Renal Calculi, Recurrence Rate and Follow-up

JOHN P. BLANDY and VILLIS R. MARSHALL
The Department of Urology, The London Hospital, London E1

Many a busy urological surgeon must wonder what he should do about following up the patient who has passed a small ureteric calculus, or from whom he has removed a moderate sized stone from the renal pelvis by a straightforward and uncomplicated pyelolithotomy. No doubt we would all agree that all these patients should undergo a screening process during which certain minimal investigations should be done. These would include repeated estimations of the plasma and urine calcium, phosphate and urate, a careful search for urinary infection and appropriate urography. To these routine tests others would add measurements of urinary oxalate and of renal tubular acidifying power, though facilities to measure oxalate are not universally available and some might question the significance of supposed renal tubular acidosis, complete or incomplete, when the kidneys are scarred, obstructed or infected. Nevertheless at the end of these preliminary screening tests we shall have discovered patients with hyperparathyroidism, uric acid stone disease, cystinuria, and anatomical anomalies leading to stagnation of urine and secondary formation of calculi (Williams, 1976). The patient with big staghorn calculi poses many other problems and requires meticulous follow-up (Singh *et al.*, 1973; Blandy and Singh, 1976).

Having eliminated patients with these known predisposing factors, there remain a large number of patients without anatomical anomalies or known metabolic defects, but amongst whom a considerable proportion will have so-called idiopathic hypercalciuria. Despite the widespread acceptance of idiopathic hypercalciuria as a real nosological entity, we have been reluctant to subject all our patients with high calcium outputs and small renal calculi to any of the various therapeutic regimens which are advocated from time to time, since in our follow-up study there was no correlation between hypercalciuria and recurrence of stones, except in one small and highly selected group of men (Marshall *et al.*, 1975). On the other hand, from the experience

Table I

Stone Cases 1967-71

Staghorns	125	23%
Anatomical abnormality	32	10%
Recumbency	10	
Hyperparathyroidism	4	
Uric acid	3	
Cystine	1	
Bladder	4	
"Idiopathic"	362	67%
All cases	541	100%

Read at the 32nd Annual Meeting of the British Association of Urological Surgeons in London, June 1976.

Table II

"Idiopathic" Stones

	Males	Females
Total in series	211	171
Hypercalciuric	112 (> 350 mg/24 hr)	39 (> 300 mg/24 hr)
Size of original stone measured	178	114

Table III

Size of Largest Stone Formed

Size	Females		Males		Both	
< 5 mm	21	18·4%	61	34·3%	82	28·0%
6-10 mm	38	33·3%	49	27·5%	87	29·8%
> 10 mm	55	48·3%	68	38·2%	123	42·2%
All cases	114		178		292	

with our stone clinic, we became more and more convinced that there was a factor of far greater significance in the long-term follow-up of the patient with a stone, and that was the *size* of the stone when it was first detected.

Ever since the early days of radiography, urologists have recognised that stones of less than 5 mm in diameter, usually pass down the ureter, and that stones greater than 10 mm in diameter usually need an operative removal. Clinically, the only problem posed by the small stone is whether to remove it when it lodges in the ureter, whereas a larger stone, particularly in a calyx, raises the question whether partial nephrectomy ought to be added to removal of the stone (Marshall *et al.*, 1976).

Once these clinical decisions have been taken, and the patient has either passed the stone or had it removed, the surgeon must decide about what kind of follow-up ought to be undertaken. This study set out to test the clinical impression that larger stones did indeed need to be followed up, but that smaller ones probably did not.

Materials (Table I)

The patients in this study consisted of 541 patients studied between 1967 and 1971 inclusive, and now followed up for more than 4 years. In this group of patients, details of whom have been previously reported (Marshall *et al.*, 1975, 1976) there were 125 patients with staghorn calculi, and 54 with obvious anatomical or metabolic causes for their stones. Excluding these, there were 362 patients with "idiopathic" stones, amongst whom hypercalciuria was present in about half the males and 25% of the females (Marshall *et al.*, 1975) (Table II).

Of the idiopathic calculi situated in the kidney there were 178 males and 114 females in whom radiographs of the original stones were available for measurement. In each of these 292 patients the longest axis of the largest of the original stones was measured to the nearest millimetre. On this basis patients were assigned to 1 of 3 groups, where the stone diameter was less than 5 mm, 6 to 10 mm, or larger than 10 mm. The methods for estimating urinary calcium, infection,

Table IV

Operation Rate and Stone Size

	Size of stone	Number of patients	Number of operations	
Females	<5 mm	21	0	0%
	6-10 mm	38	18	47·4%
	>10 mm	55	51	92·8%
Males	<5 mm	61	8	13·1%
	6-10 mm	49	24	49·0%
	>10 mm	68	59	86·7%

Table V

Size of Recurrence

	Initial stone		Recurrent stones				
			No. with recurrent stones		Sizes of recurrent stones		
	No.	Size			<5 mm	6-10 mm	>10 mm
Females	21	<5 mm	5	23·8%	**5**	0	0
	38	6-10 mm	9	23·6%	6	**9**	1
	55	>10 mm	20	36·4%	2	1	**20**
Males	61	<5 mm	24	39·4%	**24**	0	0
	49	6-10 mm	21	42·9%	15	**24**	6
	68	>10 mm	37	54·9%	9	14	**25**

recurrence rates and for calculating surface area were as described previously (Marshall *et al.*, 1975).

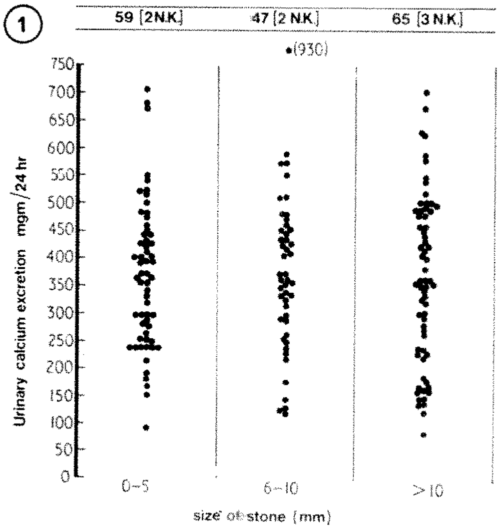
Results

While men had an even distribution of calculi in each of the 3 size groups, women tended to form larger calculi (Table III) and, as might be expected, operations were more often required when the stones were big (Table IV). In none of the 21 women with small stones was an operation needed, and in the 8 men, it consisted of a Dormia extraction or an attempt at extraction. Stones recurred more often in those patients whose first stones had been big, than when they had been small (Table V). In the 68 men whose stones were at first bigger than 10 mm in diameter no less than 25 developed recurrent stones of a size which called for a second operation. The level of urinary calcium excretion was unrelated to the initial size of the stone in men or in women (Figs. 1 and 2): nor was the surface area of the patient as calculated from height and weight (Figs. 3 and 4). Smaller stones occurred at a slightly earlier age in both men and women (Figs. 5 and 6) the difference being significant in males ($P<0{\cdot}05$) but not in females. Infection was more often found when the stones were large to start with, and continued to occur in this group of patients throughout the follow-up (Table VI) in both sexes, though less often seen in the males.

Discussion

Although we attempted to measure the size of each stone as precisely as possible, the distinction between the 3 groups in this study is of course not exact, but it does serve to distinguish those

①



②

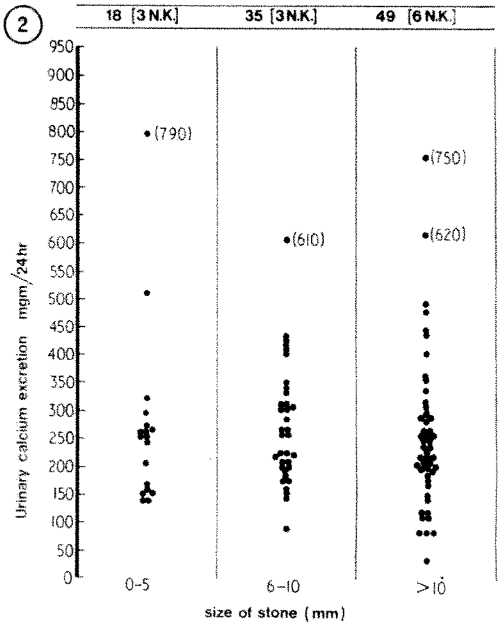
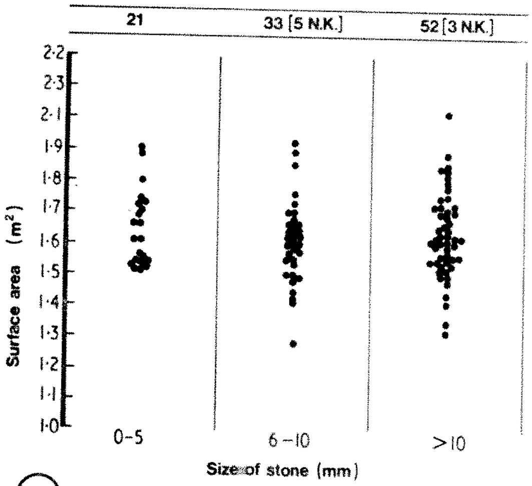
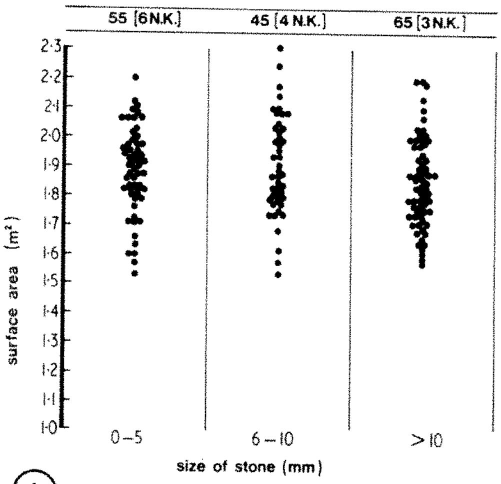


Fig. 1. Comparison of size of stone with urinary calcium excretion in 178 male patients. (NK = not known.)

Fig. 2. Comparison of size of stone with urinary calcium excretion in 114 female patients. (NK = not known.)



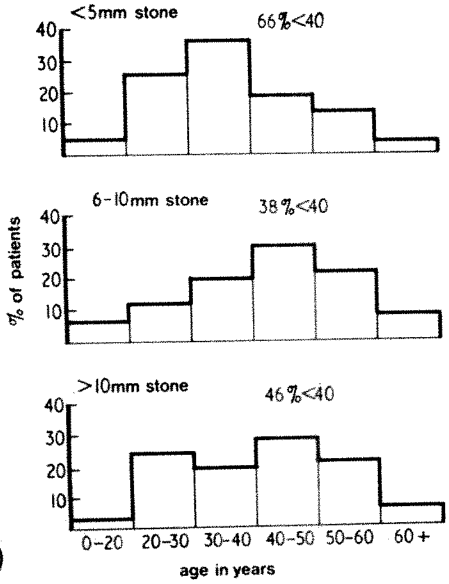
③



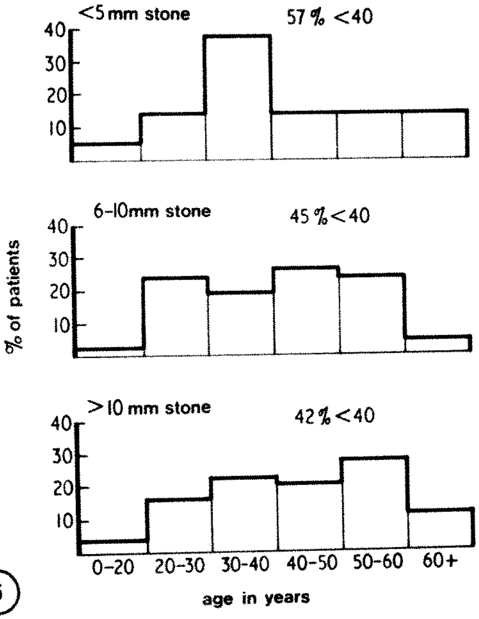
④

Fig. 3. Comparison of size of stone with surface area in 114 female patients. (NK = not known.)

Fig. 4. Comparison of size of stone with surface area in 178 male patients. (NK = not known.)



5



6

Fig. 5. Age, onset of symptoms in males.

Fig. 6. Age, onset of symptoms in females.

with small stones as a group from those with large ones. By making this distinction, not only were we able to decide which stones were likely to pass down the ureter without trouble, or with a Dormia basket, but also we were provided with useful information as to the likely fate of these patients during the period of a prolonged follow-up.

Those who present with small calculi, less than 5 mm in diameter, will usually pass them, and if they do have a recurrence, it will usually be a small one. It would seem that these are a low-risk group of patients who could be asked to come again only if their symptoms warrant further attention. It is true that amongst them there will be, as our previous study emphasised (Marshall *et al.*, 1975) a very small group of males, with a high calcium output in the urine, in whom there will be multiple recurrences. This group will soon declare itself by reason of recurrent symptoms and can then be subjected to closer scrutiny and to a more detailed follow-up: even perhaps, to therapy designed to lower the urinary level of calcium.

Patients with a stone of any size in whom there is an associated *Proteus morgani* infection deserve particular attention, for this group has a high risk of recurrence; and since these infections are often asymptomatic, it is probably wise to follow them all with care and to treat the infection appropriately.

The size of the stone when first seen appears to be a most useful index of the need for follow-up. If stones are larger than 10 mm across, then the risk of recurrence is very considerable. Perhaps surgeons should pay more attention to this simple factor, which sorts the "surgical" from the "non-surgical" stones, than to some of the biochemical measurements which, in the management of the patient often seem to be irrelevant.

Table VI

Infection and the Size of Renal and Ureteric Calculi

	Size	Number of patients	Initial infection		Subsequent infection	
Females	<5 mm	21	0	0%	1	4·8%
	6-10 mm	38	9	23·6%	14	36·8%
	>10 mm	55	27	49·1%	32	58·2%
Males	<5 mm	61	0	0%	0	0%
	6-10 mm	49	3	6·1%	1	2·0%
	>10 mm	68	4	5·9%	11	16·2%

Summary

Stones smaller than 5 mm in diameter seldom need any operation other than the use of the stone-basket.

Stones larger than 10 mm in diameter usually need an operation, are more often accompanied by infection, and have a higher recurrence rate.

The size of the stone is unrelated to the level of urinary calcium or to body surface area.

In planning the follow-up of patients with calculi the size of the first stone is a useful guide.

References

BLANDY, J. P. and SINGH, M. (1976). The case for a more aggressive approach to staghorn stones. *Journal of Urology*, **115**, 505-506.

MARSHALL, V. R., WHITE, R. H., CHAPUT DE SAINTONGE, M., TRESIDDER, G. C. and BLANDY, J. P. (1975). The natural history of renal and ureteric calculi. *British Journal of Urology*, **47**, 117-124.

MARSHALL, V. R., SINGH, M., TRESIDDER, G. C. and BLANDY, J. P. (1976). The place of partial nephrectomy in the management of renal calyceal calculi. *British Journal of Urology*, **47**, 759-764.

SINGH, M., CHAPMAN, R. H., TRESIDDER, G. C. and BLANDY, J. P. (1973). The fate of the unoperated staghorn calculus. *British Journal of Urology*, **45**, 581-585.

WILLIAMS, R. E. (1976). Renal and ureteric calculi. Chapter 14 in *Urology*, Vol. I., ed J. P. Blandy. Blackwell Scientific, Oxford, pp. 291-347.

The Authors

John P. Blandy, DM, MCh, FRCS, Professor of Urology.

Villis R. Marshall, MD, FRACS, Commonwealth Fellow in Urology (now Senior Lecturer, University of Adelaide).

British Journal of Urology (1976), **48**, 531-537 ©

Recurrence of Infected Calculi Following Postoperative Renal Irrigation with Stone Solvent

GAVIN ROYLE and JOE C. SMITH
Radcliffe Infirmary, Oxford

Infected renal calculi are notoriously prone to recurrence following surgical removal. This may be due to small particles of infected calculi left behind acting as a nidus for further stone formation. A stone solvent, Renacidin,* first described by Mulvaney (1959), has been used to try to dissolve any remaining particles.

Renacidin consists of organic acids and their salts. A 10% solution consists of D-gluconic acid 0·3%, gluconolactone 0·1%, citric acid 0·6%, magnesium citrate 5·9%, magnesium gluconocitrates 1·2%, magnesium bicarbonate 0·8% and calcium bicarbonate 0·2% with a pH of 4.

In vitro Experiments

Small pieces of infected calculi were irrigated with 10% Renacidin at 500 ml/6 hours for 40 hours. A constant flow system with the stone immersed in a gauze pouch of fine mesh (200 microns) in a constant volume of solvent was used. A system irrigated with normal saline at the same room temperature was used as a control. The gauze pouch was made from the filter chamber of an intravenous giving set.

Stones irrigated with Renacidin showed a large decrease in size (Fig. 1) with no trace of inorganic constituents after 40 hours. Only a small amount of organic debris was left. Parts of the same stones irrigated with saline showed only a minor decrease in size after 40 hours and inorganic material was still present.

Patients

34 patients with infected renal calculi were studied prospectively. 30 patients were female and 4 were male. The majority were aged 30-50 years (Fig. 2). All patients had infected urine prior to surgery and all stones cultured yielded positive cultures. *Proteus* was by far the commonest organism (Table I). All patients had normal blood calcium, alkaline phosphatase and uric acid. No abnormalities of urinary calcium or cystine excretion were found. 8 patients had bilateral calculi and 26 had unilateral calculi. All patients had symptoms of either loin pain, recurrent urinary infection or those of pyonephrosis expediting emergency admission. There was a high incidence of previous renal stone surgery—35% of the unilateral group and 25% of the bilateral group. Many of these kidneys were in poor condition. 9 patients had poor renal function (blood urea >40 mg %) prior to operation.

Read at the 32nd Annual Meeting of the British Association of Urological Surgeons in London, June 1976.

---

* Guardian Chemical Corporation, New York, USA.

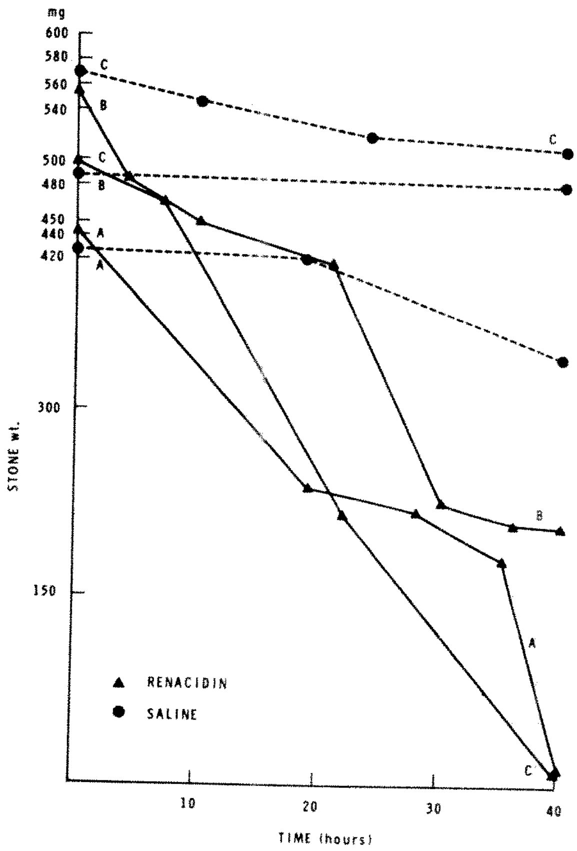


Fig. 1. *In vitro* dissolution results showing the change in stone weight after irrigation with Renacidin.

Methods

Of the 16 bilateral calculi 15 were treated by pyelolithotomy, 1 underwent nephrectomy for non-function. All 26 unilateral stones underwent pyelolithotomy. The Gil-Vernet technique was invariably used via a loin approach. Nephrolithotomy was used in addition if necessary. Per-operative renal X-rays were taken in most cases. Following pyelolithotomy a nephrostomy tube with multiple holes was left in the renal pelvis (Fig. 3, Gear and Smith, 1970). Appropriate antibiotic therapy was commenced on the day of operation and continued for at least 1 month after operation. The nephrostomy tube was allowed to drain freely until day 3 when a nephrostogram was performed to check its position. If the position was satisfactory normal saline was irrigated through the nephrostomy tube on day 4 at 500 ml/6 hours. Irrigation was performed during daylight hours only to ensure close nursing supervision. Pulse, blood pressure and temperature were recorded half-hourly and any change or the development of loin pain were indications to stop the irrigation. Patients were not confined to bed at any stage. If the normal saline irrigation was uneventful 10% Renacidin was irrigated from days 5 to 10. If closure of the pyelolithotomy was difficult, irrigation was delayed to day 7. Frequent urine cultures were made and sensitivities noted. Blood haemoglobin, white cell count, urea, creatinine and electrolytes were frequently estimated. Blood calcium, magnesium, phosphate and citrate were estimated in some patients.

All calculi removed were sent for culture as well as biochemical analysis.

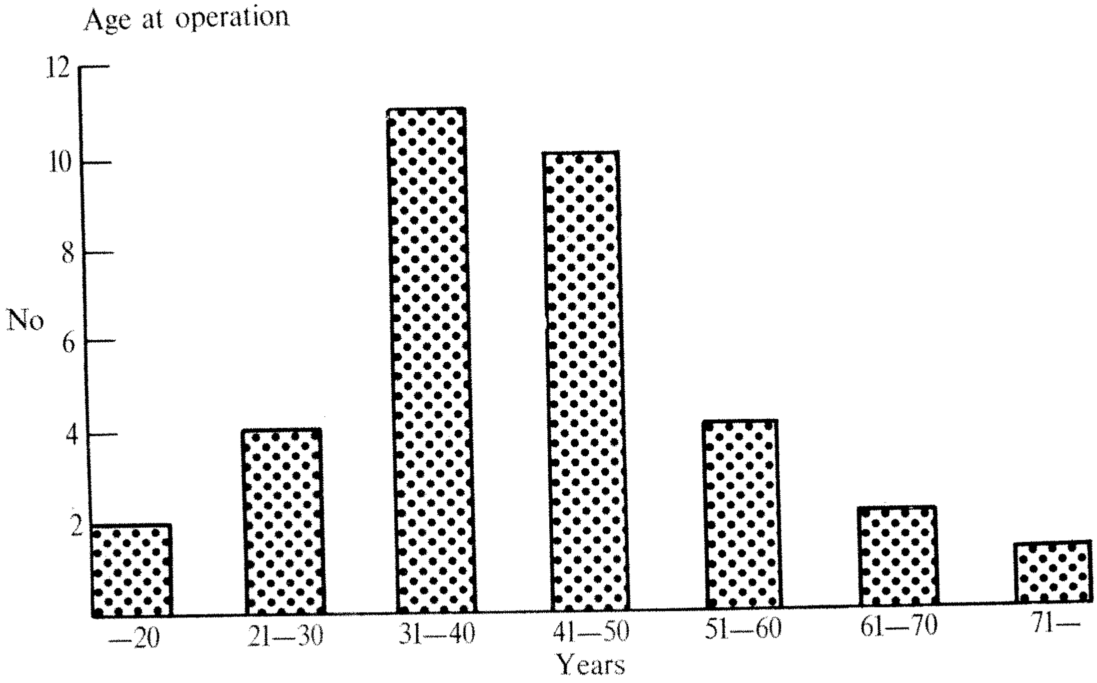


Fig. 2. Age incidence in 34 patients with infected renal calculi.

Results

(i) *Irrigations*

6 irrigations (14·6%) were abandoned either due to loin pain or leak of contrast or saline on irrigating the kidney. No increase in blood urea, creatinine, calcium, magnesium phosphate or citrate was noted during Renacidin irrigation. No case of haemorrhage, septicaemia or pyonephrosis occurred. Of the 6 cases of abandoned irrigation, 3 later developed recurrent calculi. Of the 35 successful irrigations, 7 later developed recurrent calculi.

(ii) *Renal Function*

Of the 9 patients with poor renal function prior to surgery, 7 improved, 1 remained the same and 1 deteriorated (Fig. 4). The patient whose renal function deteriorated was hypertensive, having had 1 kidney removed elsewhere for stone. Haemodialysis was begun 24 months post-pyelolithotomy. Later his remaining kidney was removed to control persistent hypertension. Histological examination of the kidney showed nephrosclerosis with no stone remaining. Of the 25 patients with normal renal function none deteriorated after operation.

(iii) *Stone Composition*

On qualitative chemical analysis all stones were of a mixed nature consisting of phosphate, oxalate, calcium and ammonium. No cystine or urate stones were found in this series of patients.

(iv) *Follow-up*

Patients were followed with regard to symptoms, blood pressure, M.S.U., blood urea, plain abdominal radiograph and where indicated excretion urography. The mean follow-up for the

Table I

Urine and Stone Culture in 34 Patients with Renal Calculi

Proteus mirabilis	21
Proteus + coliform	6
Proteus + *E. coli*	1
E. coli + *S. faecalis*	1
E. coli	1
B. aerogenes	1
Staph. aureus	1
"Coliforms"	2
	34

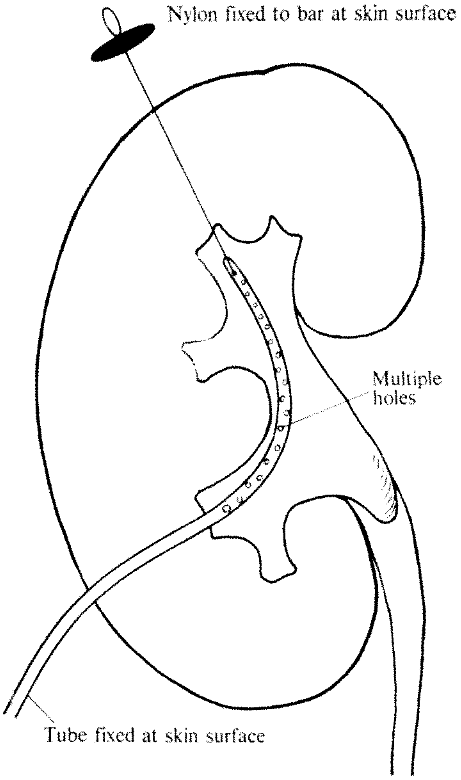

Nylon fixed to bar at skin surface
Multiple holes
Tube fixed at skin surface

Fig. 3. Position of Gear-Smith nephrostomy following pyelolithotomy.

unilateral group was 49 months. The mean follow-up for the bilateral group was 27 months. Mean overall follow-up was 42 months.

(v) *Recurrence of Stone*

4 out of 26 stones of the unilateral group recurred (15·4%). The mean time of recurrence, as judged by stone visualisation on plain abdominal radiograph, was 27 months. This includes 1 patient who defaulted from follow-up after 18 months and presented at 5 years with large recurrent calculi. The 3 other calculi that recurred were noted at 3, 11 and 36 months. None of the unilateral group formed calculi on the contralateral side. Of the 4 recurrent calculi 1 has necessitated nephrectomy and 1 has undergone repeat pyelolithotomy. The other 2 patients are under observation. 6 out of 15 of the bilateral stones undergoing pyelolithotomy recurred (40%). The mean time of recurrence was 12 months. Of the 6 recurrent calculi 2 have necessitated subsequent nephrectomy. Overall recurrence for both groups was 24·4%.

(vi) *Recurrence of Infection*

9 patients developed 1 or more postoperative urinary infections following cessation of antibiotic therapy (Table II). 6 of the infections were persistent and due to the original infecting organism. These 6 cases all ultimately developed recurrent calculi. 2 of the 3 transient urinary tract infections were due to "new" organisms and none of the 3 has developed a recurrent calculus so far. 4 cases of recurrent calculi have so far not had organisms cultured from their urine.

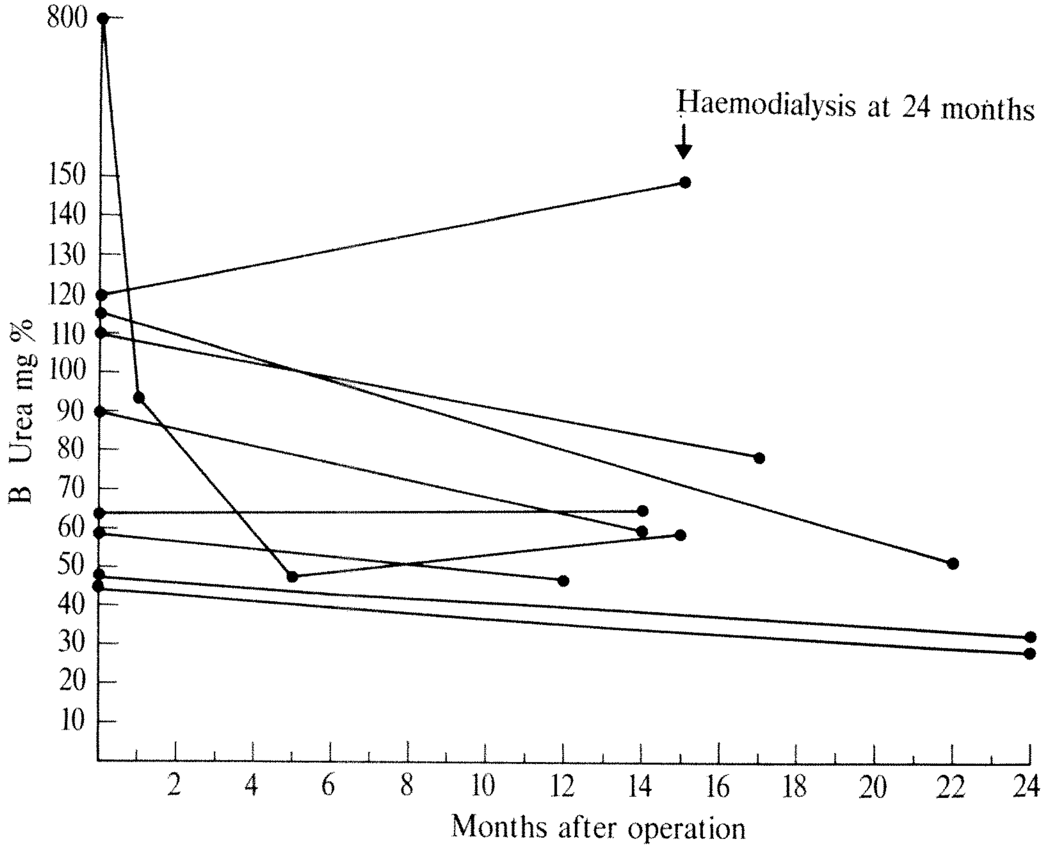


Fig. 4. Renal function (blood urea) following pyelolithotomy.

(vii) *Disappearance of Residual Calculi*

13 kidneys were left with residual calculi from evidence of per-operative renal X-rays. Following irrigation with Renacidin, 10 of these calculi were no longer seen and only 3 proceeded to increase in size to form recurrent stones.

Discussion

Following surgical removal the recurrence rate of calculi that appear to be of infective origin (*i.e.* those calculi which are associated with an infected urine and from which bacteria can be cultured) may be as high as 64% (Hellström, 1949; Sutherland, 1954; Williams, 1963).

Small or large particles left behind in the kidney following stone removal may act as a chemical or bacteriological nidus for further stone formation. *Proteus* which infected 28 out of 34 cases in our series is well known for its urea splitting properties. *Staphylococcus aureus* which occurred in 1 case may also split urea.

Methods have been introduced to improve the results of stone removal. Gil-Vernet (1965) introduced extended pyelolithotomy. Wickham (1968) demonstrated the value of renal cooling. Nephroscopy is a more recent innovation. These techniques were developed to assist removal of larger fragments of stone. Undoubtedly neither uncalcified stone matrix nor tiny particles will be seen on radiographs. Mulvaney (1959) introduced the stone solvent, Renacidin, for the

Table II

Incidence of Urinary Infection after Operation

	Total	With original organism	With different organism	With recurrent stone
Solitary	3	1	2	0
Persistent	6	6	0	6
Total	9	7	2	6

dissolution of urinary tract calculi by local irrigation and it is mainly effective in dissolving struvite ($Mg\ NH_4$, $PO_4\ 6H_2O$) and apatite ($Ca_{10}(PO_4)_6\ (OH)_2$) stones. It has little effect on oxalate, urate or cystine calculi. Its main action is probably by simple dissolution in an acid medium though a magnesium calcium ion exchange had also been postulated. Renacidin appears to be better than other solutions such as Suby's solution G both with regard to dissolution of calculi and irritation of the urinary tract.

4 reported deaths associated with the use of Renacidin caused the Food and Drug Administration to withdraw Renacidin from use in the renal pelvis in the United States. However, when Nemoy and Stamey (1971) reviewed these cases, the cause of death appeared to be sepsis associated with an infected urine. They also reported a series of 14 patients of their own with "infective" renal calculi. 8 patients were treated with Renacidin either via a nephrostomy following pyelolithotomy or by irrigation via a ureteric catheter. No recurrence of stone was reported at a follow-up of 34 months. 1 patient with a catheter had a urinary tract infection at his last follow-up. 1 patient suffered bladder irritation from Renacidin irrigation. Recently Jacobs and Gittes (1976) have reported 14 cases of renal stone treated by postoperative kidney irrigation with Renacidin. 13 appeared to be of infective origin. 12 of the cases have been followed for 17 months, 2 having defaulted. No patient is reported having recurrent calculi as yet though 1 has had recurrent urinary tract infections. Of the 15 renal irrigations in their series 7 were associated with minor complications *e.g.* pyrexia, bladder irritation and 1 was associated with a rise in creatinine associated with Kanamycin therapy. This is a high rate of complication compared with our series (15%). A Gear-Smith nephrostomy tube is probably less damaging to renal tissue and less liable to cause extravasation of irrigating fluid than a conventional nephrostomy tube as apparently used in Jacobs and Gittes's series. It is known that the longer the follow-up of renal calculi the higher the number of recurrent calculi. This may partly explain our overall recurrence rate of 24·4% at 42 months compared with the results of Nemoy and Stamey and Jacobs and Gittes. For example the mean time of recurrence of our unilateral group of stones was 27 months. Overall follow-up of Jacobs and Gittes's patients has so far only reached 17 months.

Many of the kidneys in our series were in poor condition—31% had undergone previous operations elsewhere. This may have led to both failure of removal of stone at operation and failure of solvent to reach residual calculi postoperatively. Kidneys that developed recurrent calculi were in such poor condition in some cases that nephrectomy was indicated in 3 and as a primary procedure in 1. 1 patient though not a recurrent stone former has come to haemodialysis. Poor renal function may partly explain the high rate of recurrence of calculi in our bilateral stone group compared with the unilateral group—40 *vs.* 15·4%. 4 (50%) of the bilateral group had poor renal function. Gross renal destruction in some of these patients might have warranted nephrectomy had the contralateral kidney been normal. Finally, following operation on 1 side the calculus on the other side will act as a septic focus until it too is removed. All bilateral calculi in this series were removed on separate occasions up to 6 months apart.

From our series it appears that Renacidin is safe provided that its administration is closely monitored and is covered by the appropriate antibiotic. Our results indicate that Renacidin may have a place in the adjuvant treatment of infected renal calculi.

Summary

Renacidin has been shown to dissolve small fragments of infected renal calculi *in vitro*.

34 patients with infected calculi have undergone pyelolithotomy and postoperative renal irrigation with Renacidin. 30 patients were women and *Proteus* was the commonest infecting organism.

Renal irrigation appears to be safe if closely monitored and covered by antibiotic therapy. 24·4% of calculi had recurred at a mean follow-up of 42 months. The rate of recurrence or unilateral calculi was much less than that of bilateral calculi (15% *vs.* 40%). Persistent postoperative urinary tract infections later led to recurrent stone formation.

References

GEAR, M. and SMITH, J. C. (1970). Two techniques for nephrostomy. *Journal of Urology*, **103**, 425.

GIL-VERNET, J. (1965). New surgical concepts in removing renal calculi. *Urologia Internationalis*, **20**, 255-288.

HELLSTRÖM, J. (1949). Aetiological and therapeutic experiences concerning kidney and ureteric stones. *British Journal of Urology*, **21**, 9-16.

JACOBS, S. C. and GITTES, R. F. (1976). Dissolution of residual renal calculi with hemiacidrin. *Journal of Urology*, **115**, 2-4.

MULVANEY, W. P. (1959). A new solvent for certain urinary calculi: a preliminary report. *Journal of Urology*, **82**, 546-548.

NEMOY, N. J. and STAMEY, T. A. (1971). Surgical, bacteriological and biochemical management of "infection stones". *Journal of the American Medical Association*, **215**, 1470-1476.

SUTHERLAND, J. W. (1954). Recurrence following operations for upper urinary tract stone. *British Journal of Urology*, **26**, 22-45.

WICKHAM, J. E. A. (1968). A simple method for regional renal hypothermia. *Journal of Urology*, **99**, 246-247.

WILLIAMS, R. E. (1963). Long term survey of 538 patients with upper urinary tract stone. *British Journal of Urology*, **35**, 416-437.

The Authors

G. T. Royle, FRCS, Surgical Registrar.
J. C. Smith, MS, FRCS, Consultant Surgeon and Urologist.

Requests for reprints to be sent to Mr J. C. Smith.

British Journal of Urology (1976), **48**, 539-548 ©

Primary Hyperparathyroidism—A Review of Cases in the Sheffield Area

J. C. HAMMONDS, J. L. WILLIAMS and L. HARVEY
Department of Urology, Hallamshire Hospital, Sheffield

The association of a tumour in the neck with the classical bone changes of von Recklinghausen was first reported in 1904 but it was not until 1925 that the first parathyroidectomy was performed in Vienna (Mandl, 1926). In the same year parathyroid hormone was extracted from bovine parathyroid glands by Collip (1925) and its hypocalcaemic properties demonstrated in dogs. The association of hyperparathyroidism with renal stones was recognised in 1932 (Cope, 1966) and since that time the association between peptic ulceration (Rogers *et al.*, 1947) pancreatitis (Cope *et al.*, 1957) and hypertension (Hellstrom, Birke and Edvall, 1958) has been reported in patients with hyperparathyroidism.

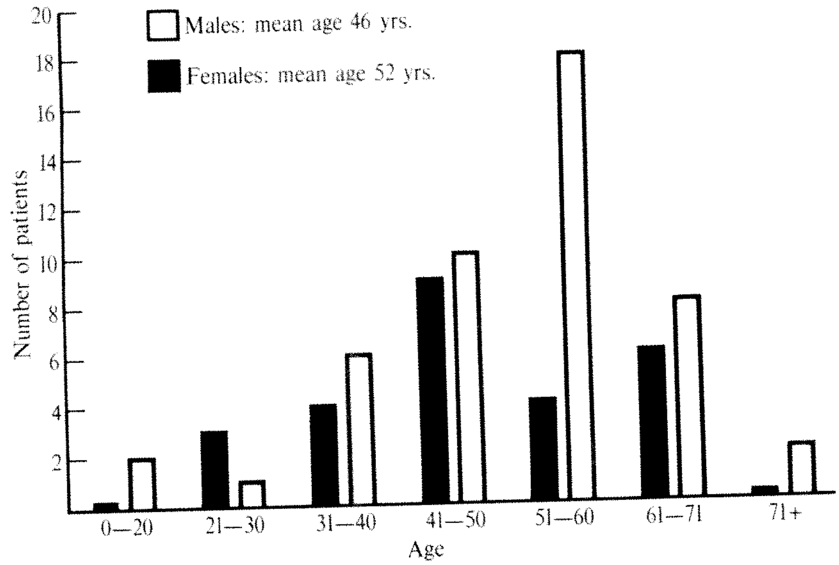


Fig. 1. Age distribution of patients with hyperparathyroidism.

Until recently, hyperparathyroidism has been considered to be a rare disease, large series of cases being collected by a few centres with a special interest in the problem (Cope, 1966; Purnell *et al.*, 1974; Watson, 1974).

After re-examining histological material submitted to the pathology department from 1955 to 1976, 97 patients were found to have abnormal parathyroid tissue. Patients with secondary

Read at the 32nd Annual Meeting of the British Association of Urological Surgeons in London, June 1976.

Table I

Presentation in 73 Patients

	%
Renal stones	46 (63)
Skeletal changes	9 (12)
Abdominal pain	4 (6)
Hypercalcaemia	6 (8)
Hypertension	2 (3)
Chance finding	6 (8)

Table II

Associated Symptoms

	Total cases (%)
Nocturia	41
Hypertension	25
Abdominal pain	24
Constipation	23
Depression	17
Headache	10
Polyuria	10
Muscular weakness	8

Table III

Distribution of Stones

Renal	
Unilateral	20
Bilateral	11
Nephrocalcinosis	1
Renal + ureteric	14
Ureteric	10
Bladder	1

and tertiary hyperparathyroidism have been excluded as they were too few to be submitted to meaningful analysis. The records of 73 patients with primary hyperparathyroidism have been traced and the information is presented here.

Patients

There were 26 males and 47 females (Fig. 1). The mean age was 46 years for men and 52 years for women.

The majority of patients presented with symptoms due to urinary calculi (Table I). 9 presented with skeletal changes. 6 of these had generalised bone pains; 2 pathological fractures of the femur and 1 an expanding giant-cell lesion in the jaw. Of the 4 patients who presented with abdominal pain, only 1 had a peptic ulcer and none had pancreatitis. 6 patients presented with hypercalcaemic symptoms of polyuria, thirst and vague abdominal discomfort. 1 patient required urgent correction of hypercalcaemia before surgery. 2 patients were found to have hypercalcaemia during investigation for their hypertension and 6 others while being investigated for unrelated problems.

Associated symptoms are summarised in Table II. 41% had significant nocturia, voiding at least twice in the night although diurnal frequency was unusual.

57 patients (78%) had urinary calculi but only 51 of these had symptoms referrable to them. 77% of these patients had multiple stones or nephrocalcinosis compared with only 45% of a series of 100 consecutive stone formers in Sheffield.

The anatomical distribution of stones is shown in Table III, the majority being renal.

22 patients had a history of stones for 2 to 20 years before the diagnosis was made. During this time recurrent stones had formed in 16 (73%). Following correction of the hyperparathyroidism new stones formed in only 5 (9%) of the 57 patients.

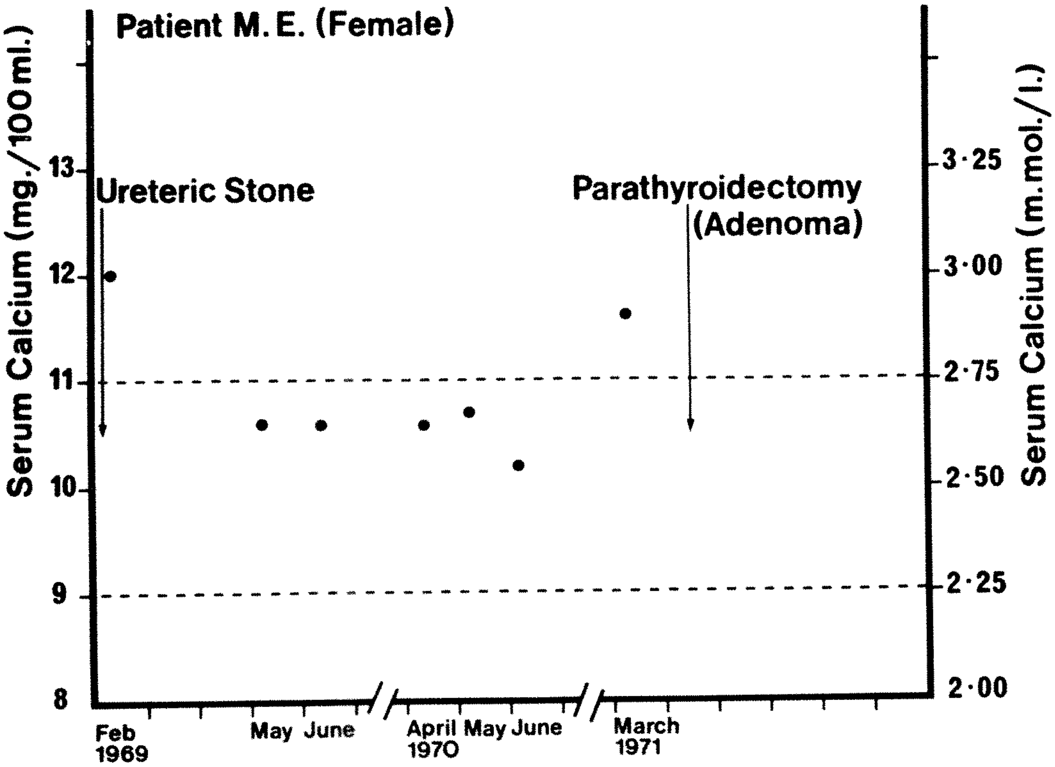


Fig. 2. Serial serum calcium levels in a patient with hyperparathyroidism.

Diagnosis

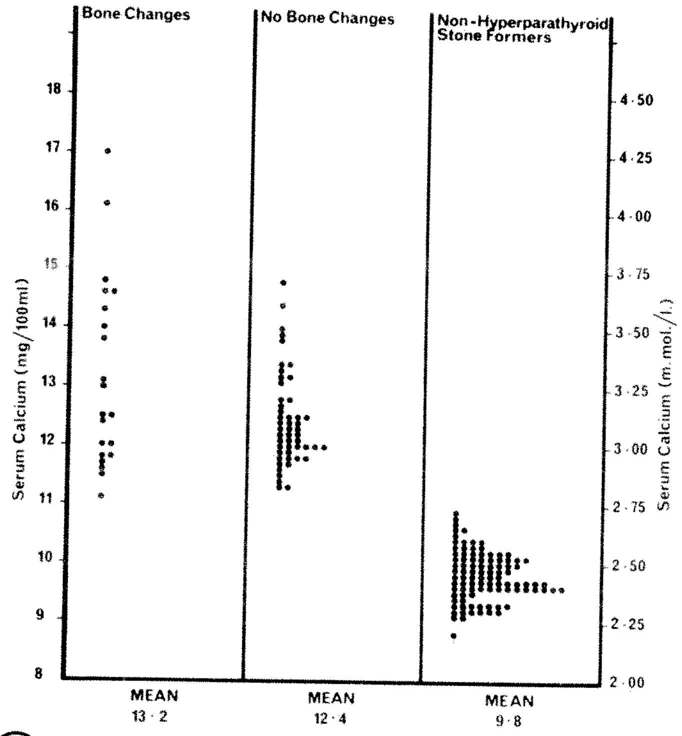
In each case the most important diagnostic index was the serum calcium which is corrected for serum protein levels. Within the normal range quoted by our laboratories, 51 patients had persistent hypercalcaemia until parathyroidectomy was performed. However 22 patients had intermittent hypercalcaemia, the clinical course of 1 such patient being represented in Figure 2. In Figure 3 the highest serum calcium level recorded in all patients with primary hyperparathyroidism is compared with the highest serum calcium level in a group of non-hyperparathyroid stone formers. Figure 4 shows the lowest recorded serum calcium for each patient. Patients with radiological evidence of bone changes have somewhat higher calcium levels than patients without such changes.

Hypercalciuria was a common finding although there was a large overlap with a series of non-hyperparathyroid stone formers and approximately 1 in 5 patients had normal calcium excretions (Fig. 5).

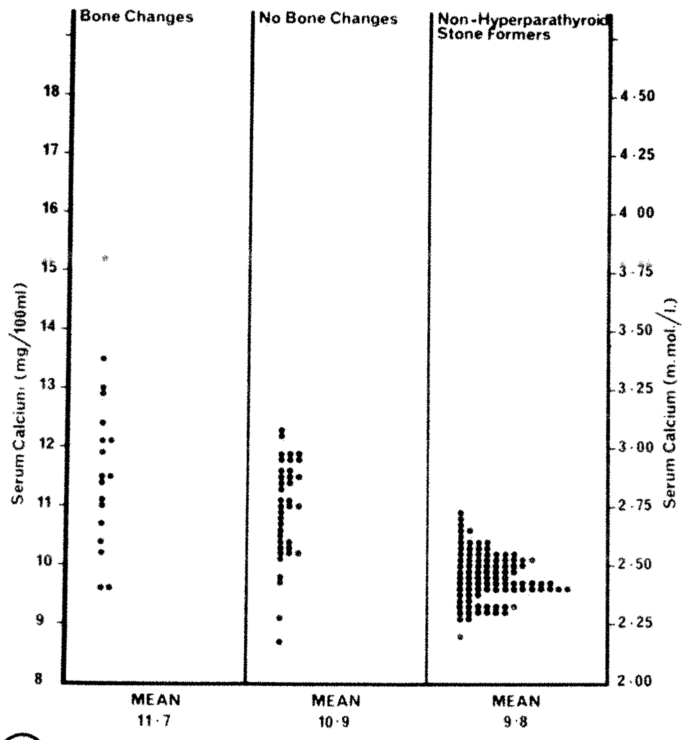
The serum phosphate was an unreliable diagnostic index in this series (Fig. 6) and was probably higher than expected (Watson, 1974). Serum should be rapidly separated from erythrocytes to prevent leakage of intracellular phosphate if true values are to be obtained.

Plasma chloride was measured in only a small number of cases but in no instance was the level less than 101 mEq/l.

Elevated levels of serum alkaline phosphatase were found in patients with and without radiological evidence of bone disease, although the proportion of those with an elevated level was greater in patients with bone changes (Table IV).



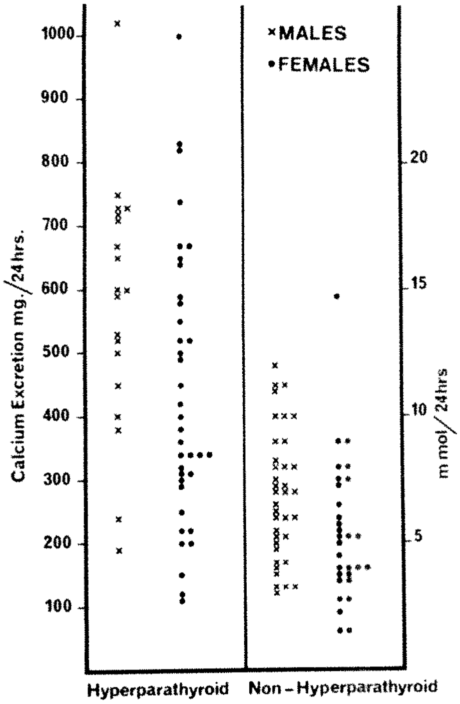
3



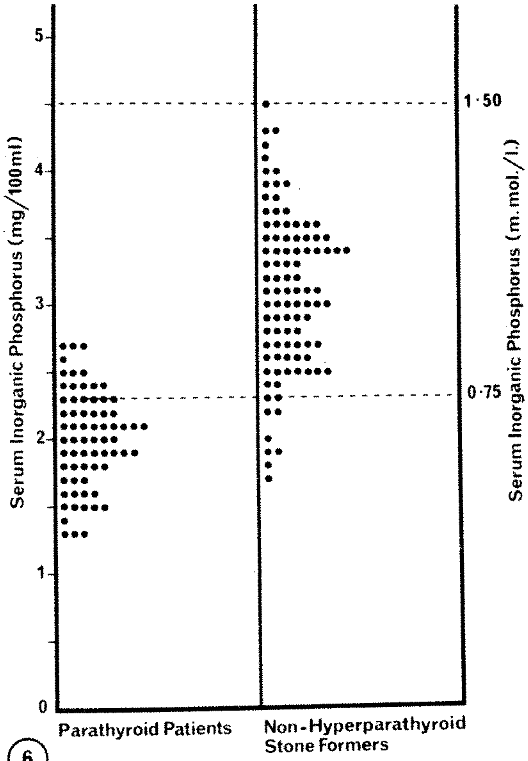
4

Fig. 3 Highest recorded serum calcium in hyperparathyroid patients and a series of non-hyperparathyroid stone formers.

Fig. 4. Lowest recorded serum calcium in hyperparathyroid patients and a series of non-hyperparathyroid stone formers.



⑤



⑥

Fig. 5. Urinary calcium excretion in hyperparathyroid patients and a series of non-hyperparathyroid stone formers.

Fig. 6. The distribution of serum inorganic phosphorus in hyperparathyroid patients and a series of non-hyperparathyroid stone formers.

Parathyroid hormone was estimated by radioimmunoassay, in the peripheral venous blood of 22 patients. An elevated level was observed in 15 and in 7 (32%) the level was misleadingly low or undetectable. Assay by multiple sampling from the large neck veins was performed in 7 patients, the tumour being accurately located in 5.

49 patients were examined for radiological evidence of bone disease, definite bone changes being seen in only 43%.

Surgery

The neck was explored in all cases. Recently we have used intravenous methylene blue as a means of identifying abnormal parathyroid tissue (Dudley, 1971). This technique was felt to have been helpful in the rapid identification of parathyroid tumours in 12 out of 14 patients.

True mediastinal tumours were not encountered in this series although in several instances the tumour was partially situated in the upper mediastinum but could easily be delivered through the cervical incision. The distribution of adenomas in the neck is shown in Table V. The lower parathyroids were involved most frequently and there appears to be a difference in lateralisation between males and females.

Table IV

Serum Alkaline Phosphatase

	Bone changes	No bone changes
Normal level	5	22
Elevated level	16	14

Table V

Distribution of Adenomas in the Neck

	Males		Females	
	Right	Left	Right	Left
Upper	5	3	2	5
Lower	12	6	12	26

Table VI

Histology

Adenoma	
Chief cell	28
Clear cell	22
Oxyphil cell	6
Unclassified	12
Hyperplasia	
Chief cell	3
Clear cell	1
Carcinoma	1

Table VII

Postoperative Serum Calcium

Total patients		73
Normocalcaemic	66	
Hypocalcaemic	5	
Hypercalcaemic	2	

There was no mortality associated with surgery. 4 patients developed a wound infection or haematoma. Immediate short-lived hypocalcaemia was common but tetany occurred in only 1 patient.

Pathology

Most of the patients had adenomas (Table VI). Histologically the majority were chief or clear cell, but there were 6 oxyphil tumours. Hyperplasia involved all 4 glands in 3 patients but only 2 glands in 1. 1 patient had a carcinoma of the parathyroid.

The weight of tissue removed varied from 150 mg to 8 g. There was no difference between the sexes or between patients with or without bone changes. A loose relationship exists between tumour size and serum calcium level (Fig. 7).

Results

69 patients were cured by a single operation. 1 patient had an initial negative exploration but an adenoma was found 6 months later. A further patient had recurrence of hypercalcaemia after a right lower parathyroid adenoma had been removed. Re-exploration 6 years later revealed hyperplasia of the upper parathyroids. 2 patients had persistent hypercalcaemia. 1 of these had a parathyroid carcinoma with local recurrence and the other was lost to follow-up.

The postoperative calcium status is shown in Table VII. 5 patients who developed prolonged hypocalcaemia required out-patient calcium therapy. In each case at least 2 normal parathyroids were seen and preserved when the neck was explored.

Following correction of the hyperparathyroidism, the calcium excretion of 15 patients who were previously hypercalciuric, fell towards normal levels (Fig. 8). In 5 patients who formed recurrent stones after parathyroidectomy, the postoperative calcium excretion was normal.

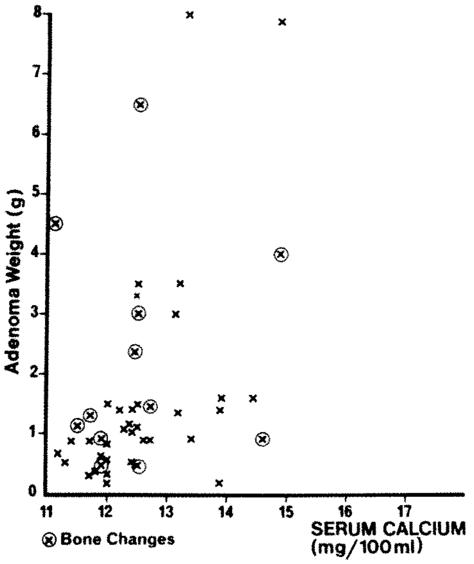
Discussion

Primary hyperparathyroidism is a disease with a peak incidence in the fifth decade affecting women approximately twice as often as men (Cope, 1966; Pyrah, Hodgkinson and Anderson, 1966; Watson, 1974). The age range is, however, wide and cases have been reported in children (Nolan, Hayles and Woolmer, 1960).

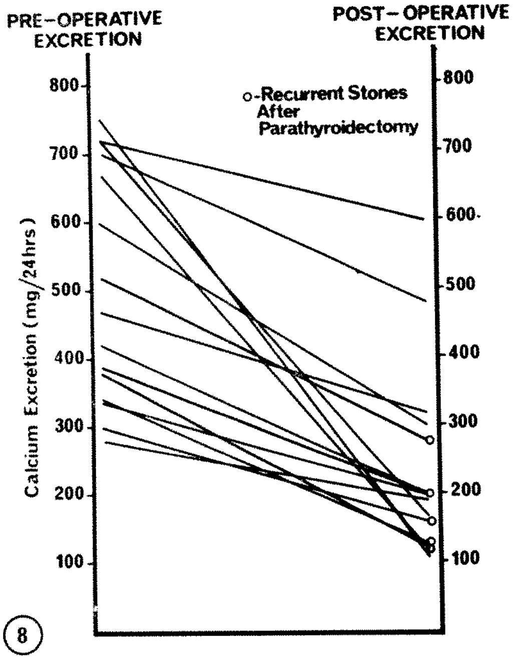
Bone disease was the predominant presenting feature earlier in the century and has now given way to calculous disease of the urinary tract which accounted for 63 % of the presenting symptoms in this series. Stones associated with hyperparathyroidism are more likely to be multiple (Pyrah *et al.*, 1966) and recurrent (McGeown, 1961). 45 % of stones in non-hyperparathyroid patients in Sheffield are multiple contrasting with 77 % in this series. The reduction of recurrent stone formation from 73 % to 9 % after parathyroidectomy lends support to the findings of McGeown (1961) who showed by statistical analysis, a reduction in the rate of recurrent stone formation after correction of hyperparathyroidism.

Few of our patients had peptic ulcers although an association between hyperparathyroidism and peptic ulceration was noted by Rogers *et al.* (1947). It is possible that the association is valid only in the more uncommon condition of multiple endocrine adenomas (Reiss and Canterbury, 1974). Abdominal pain of undefined aetiology is more common (Watson, 1974) and in half our patients with this symptom there was an immediate dramatic relief following parathyroidectomy. We have not observed pancreatitis in association with hyperparathyroidism although it was diagnosed in 7 % of a series of 155 cases from the Massachusetts General Hospital (Mixter, Keynes and Cope, 1962).

25 % of our patients were hypertensive. Hellstrom *et al.* (1958) found hypertension in 70 %



⑦



⑧

Fig. 7. The correlation between adenoma weight and serum calcium in hyperparathyroid patients. Patients with radiological evidence of bone change are indicated by a ringed cross.

Fig. 8. Urinary calcium excretion in hyperparathyroid patients before and after parathyroidectomy.

of patients with hyperparathyroidism the hypertension being related to impaired renal function. Although the blood pressure may show a transient fall when the hyperparathyroidism is corrected, it usually persists (Watson, 1974).

Polyuria, due to disturbance of tubular function, may in severe cases mimic diabetes insipidus (Pyrah *et al.*, 1966). Only 10% of our patients complained of polyuria although 41% had nocturia, presumably an earlier manifestation of the same symptom.

The serum calcium was the most important diagnostic index exceeding 11 mg/100 ml in every case in this series. The normal range is stated to be 9 mg to 11 mg/100 ml (2·25-2·75 mmol/l.). A true normal range should be determined by each laboratory by sampling from the normal population. When this has been done in centres with a special interest in calcium metabolism the normal range has been much narrower, with lower upper limits. If the wider limits are accepted then marginal hypercalcaemia will be missed. 30% of the patients in our series had normal serum calcium levels at times before the diagnosis was made. Similar findings have been reported by others (McGeown and Morrison, 1959; Riddick and Reiss, 1962). Repeated calcium estimations are therefore necessary in all patients with stones.

In a review of 138 patients, Lloyd (1968) reported a definite correlation between tumour size and serum calcium levels. Also, in his patients with overt bone disease, the tumours were larger, the serum calcium higher and the history shorter than in patients with stones. We were only able to find some relationship between serum calcium and tumour size.

Hypercalciuria was common although approximately 1 in every 5 patients had normal levels. Parathyroid hormone has been shown to promote significant tubular reabsorption of calcium (Nordin and Peacock, 1969). In patients with hyperparathyroidism this action of parathyroid hormone compensates for the increased filtered load of calcium resulting in normal calcium excretion in some of these patients. Hypercalciuria was also a poor diagnostic index owing to the overlap with other stone formers, approximately one-third of whom have hypercalciuria (Fig. 5; Williams and Chisholm, 1974).

The plasma chloride may be useful in the differential diagnosis of patients with hypercalcaemia. Parathyroid hormone acts on the renal tubules to promote bicarbonate loss resulting in a hyperchloraemic acidosis in primary hyperparathyroidism. Hypercalcaemia due to other causes promotes potassium and chloride loss. Serum chloride levels above 102 mEq/l. have been found in hyperparathyroidism and below this level in patients with hypercalcaemia due to other causes (Wills and McGowan, 1963).

The serum radioimmunoassay of parathyroid hormone was introduced by Berson *et al.* (1963) and early reports suggested that all patients with hyperparathyroidism had elevated levels (Reiss and Canterbury, 1969). However, it is our experience and that of others (Watson, 1974) that in a proportion of cases elevated levels cannot be detected. Sampling from the large neck veins has improved the technique (Reitz *et al.*, 1969) and permitted localisation of some tumours. However, owing to the variability of the venous drainage of the parathyroids and streaming of blood, this technique is less reliable than might be expected (O'Riordan, Kendall and Woodhead, 1971). We have no experience of thyroid vein catheterisation which is said to improve the results (Shimkin *et al.*, 1972). The technique of venous catheterisation is not without risk and should be reserved to help localisation in patients who have undergone previous neck surgery.

Surgical exploration can be difficult (Davies, 1974). We have been fortunate in relieving the hyperparathyroidism in 95% of patients following the first operation. Methylene blue is a useful adjunct to finding the abnormal glands.

The histology is similar to that described in other large series. The oxyphil cell adenoma is of some interest. Christie (1967) reviewed the oxyphil cell and noted its rarity in the infant parathyroid and its increasing numbers with age and in chronic renal failure. He thought that the oxyphil cell adenoma was not associated with a clinical syndrome. Oxyphil cell adenomas have, however, been reported in association with hyperparathyroidism (Selzman and Fechner, 1967) and were found in 8% of our series.

The majority of tumours involve the lower parathyroids (Nicholson, 1969). We have found no reference in the world literature to the difference in lateralisation between the sexes noted in our series.

Primary hyperparathyroidism has been considered to be a rare disease but this may be that until recently we have only observed the clinical tip of a biochemical iceberg. In large-scale screening programmes of apparently healthy populations, biochemical hyperparathyroidism has been diagnosed in 0·1% (Boonstra and Jackson, 1971; Watson, 1974). With the increasing use of multichannel analysers it is likely that primary hyperparathyroidism will be diagnosed with increasing frequency and the treatment of asymptomatic cases will become a problem. There can be no doubt that correction of the condition reduces the high recurrence rate of stone formation. The treatment of asymptomatic cases without stones is a difficult problem which will be resolved only by long-term prospective trials keeping such patients under review.

Summary

73 patients with primary hyperparathyroidism are reviewed.

The elevated serum calcium was the main diagnostic index but estimation of the parathyroid hormone was useful confirmatory evidence when raised. A normal level does not exclude the diagnosis being found in 32% of patients.

Intravenous methylene blue was a useful adjunct to surgery.

95% of the patients had relief of their hypercalcaemia after a single operation.

78% of patients had stones and there was a marked reduction in further stone formation after surgery.

We are particularly indebted to Mr C. H. Talbot, who operated on a large number of patients in this series, to Professor T. J. Martin for his helpful comments and for the parathyroid hormone assays, and to the following surgeons who kindly allowed us to include their patients in this series: Professor R. G. Clarke; Mr Miles Fox; Mr P. Muller; Mr D. J. Robertson; and Mr J. T. Rowling.

References

BERSON, S. A., YALOW, R. S., AURBACH, G. D. and POTTS, J. T. (1963). Immunoassay of bovine and human parathyroid hormone. *Proceedings of the National Academy of Sciences*, **49**, 613-617.

BOONSTRA, C. E. and JACKSON, C. E. (1971) Serum calcium survey for hyperparathyroidism. *American Journal of Clinical Pathology*, **55**, 523-526.

CHRISTIE, A. C. (1967). The parathyroid oxyphil cells. *Journal of Clinical Pathology*, **20**, 591-602.

COLLIP, J. B. (1925). The extraction of a parathyroid hormone which will prevent or control parathyroid tetany and which regulates the level of blood calcium. *Journal of Biological Chemistry*, **63**, 395-438.

COPE, O. (1966). The story of hyperparathyroidism at the Massachusetts General Hospital. *New England Journal of Medicine*, **274**, 1174-1182.

COPE, O., CULVER, P. J., MIXTER, C. G. and NARDI, G. L. (1957). Pancreatitis, a diagnostic clue to hyperparathyroidism. *Annals of Surgery*, **145**, 857-863.

DAVIES, D. R. (1974). The surgery of primary hyperparathyroidism. *Clinics in Endocrinology and Metabolism*, **3**, 253-265.

DUDLEY, N. E. (1971). Methylene blue for rapid identification of the parathyroids. *British Medical Journal*, **3**, 680-681.

HELLSTROM, J., BIRKE, G. and EDVALL, C A. (1958). Hypertension in hyperparathyroidism. *British Journal of Urology*, **30**, 13-24.

LLOYD, H. M. (1968). Primary hyperparathyroidism: an analysis of the role of the parathyroid tumor. *Medicine*, **47**, 53-71.

MANDL, F. (1926). Klinisches und Experimentelles zur Frage der lokalisierten und generalisierten Ostitis Fibrosa. *Archiv für Klinische Chirurgie*, **143**, 1-46.

MCGEOWN, M. G. and MORRISON, E. (1959). Hyperparathyroidism. *Postgraduate Medical Journal*, **35**, 330-337.

MCGEOWN, M. G. (1961). Effect of parathyroidectomy on the incidence of renal calculi. *Lancet*, **1**, 586-587.

MIXTER, C. G., KEYNES, W. M. and COPE, O. (1962). Further experience with pancreatitis as a diagnostic clue to hyperparathyroidism. *New England Jornal of Medicine*, **266**, 265-272.

NICHOLSON, W. F. (1969). Results of parathyroidectomy. *British Journal of Surgery*, **56**, 106-108.

NOLAN, R. B., HAYLES, A. B. and WOOLNER, L. B. (1960). Adenoma of the parathyroid gland in children. Report of case and brief review of the literature. *American Journal of Diseases of Children*, **99**, 622-627.

NORDIN, B. E. C. and PEACOCK, M. (1969). Role of kidney in regulation of plasma-calcium. *Lancet*, **2**, 1280-1282.

O'RIORDAN, J. L. H., KENDALL, B. E. and WOODHEAD, J. S. (1971). Preoperative localisation of parathyroid tumours. *Lancet*, **2**, 1172-1175.

PURNELL, D. C., SCHOLZ, D. A., SMITH, L. H., SIZEMORE, G. W., BLACK, B. M., GOLDSMITH, R. S. and ARNAUD, C. D. (1974). Treatment of primary hyperparathyroidism. *American Journal of Medicine*, **56**, 800-809.

PYRAH, L. N., HODGKINSON, A. and ANDERSON, C. K. (1966). Primary hyperparathyroidism, a critical review. *British Journal of Surgery*, **53**, 245-316.

REISS, E. and CANTERBURY, J. M. (1969). Primary hyperparathyroidism. Application of radioimmunoassay to the differentiation of adenoma and hyperplasia and the preoperative localisation of hyperfunctioning parathyroid gland. *New England Journal of Medicine*, **280**, 1381-1385.

REISS, E. and CANTERBURY, J. M. (1974). Spectrum of hyperparathyroidism. *American Journal of Medicine*, **56**, 794-799.

REITZ, R. E., POLLARD, J. J., WANG, C. A., FLEISCHLI, D. J., COPE, O., MURRAY, T. M., DEFTOS, L. J. and POTTS, J. T. (1969). Localization of parathyroid adenomas by selective catheterization and radioimmunoassay. *New England Journal of Medicine*, **281**, 348-351.

RIDDICK, F. A. and REISS, E. (1962). Hyperparathyroidism: analysis of recent experiences, clinical spectrum and diagnostic tests. *Annals of Internal Medicine*, **56**, 183-197.

ROGERS, H. M., KEATING, F. R. C., MORLOCK, C. G. and BARKER, N. W. (1947). Primary hypertrophy and hyperplasia of the parathyroid glands associated with duodenal ulcer. *Archives of Internal Medicine*, **79**, 307-321.

SELZMAN, H. M. and FECHNER, R. E. (1967). Oxyphil adenoma and primary hyperparathyroidism. *Journal of the American Medical Association*, **199**, 359-361.

SHIMKIN, P. M., POWELL, D., DOPPMAN, J. L., MARX, S. J., PEARSON, K. D., WELLS, S. and KETCHAM, A. S. (1972). Parathyroid venous sampling. *Radiology*, **104**, 571-574.

WATSON, L. (1974). Primary hyperparathyroidism. *Clinics in Endocrinology and Metabolism*, **3**, 215-235.

WILLIAMS, G. and CHISHOLM, G. D. (1975). Stone screening and follow-up are necessary? *British Journal of Urology*, **47**, 745-750.

WILLS, M. R. and McGOWAN, G. K. (1964). Plasma-chloride levels in hyperparathyroidism and other hypercalcaemic states. *British Medical Journal*, **2**, 1153-1156.

The Authors

J. C. Hammonds, FRCS, Senior Registrar.
J. L. Williams, FRCS, Consultant Urologist.
L. Harvey, BA, Medical Student.

British Journal of Urology (1976), **48**, 549-554 ©

Primary Pelvic Hydronephrosis in Children: A Retrospective Survey

PATRICK SMITH, MICHAEL ROBERTS, ROBERT H. WHITAKER and ABDEL RAOUF GAROUSCHE

Departments of Urology, St Martin's Hospital, Bath, Bristol Royal Infirmary and Addenbrooke's Hospital, Cambridge

In a previous study of primary pelvic hydronephrosis affecting 200 patients of all ages (Roberts and Slade, 1964) certain features of management were discussed. It was decided to repeat this retrospective study on patients under the age of 16 years presenting in the Bristol, Bath and Cambridge areas. Patients in the latter 2 centres were derived from a 3-year period and those from Bristol from a 10-year period. The study was confined to children requiring treatment for primary pelvic hydronephrosis by which we mean pelvi-ureteric obstruction.

Patients

63 children were reviewed. In 11 cases the condition was bilateral making a total of 74 hydronephrotic kidneys. Of the unilateral cases the left side predominated by 38:14. The distribution of age at the time of presentation is shown in Figure 1 which also demonstrates the greater incidence of male children afflicted. In 3 cases of unilateral obstruction the management was complicated by there being either malformation or absence of the contralateral kidney.

Symptomatology

Loin pain was the commonest symptom but generalised abdominal pain and haematuria were also important presenting features in this series (Table I). Urinary infection was the main presenting feature in 21 cases and, as will be discussed later, this was reflected by a greater incidence of postoperative infection. The commonest infecting organisms were *E. coli* and *Proteus*. The infection usually presented with generalised symptoms, pyrexia and on several occasions with febrile convulsions. In 3 children acute symptoms were not present and the hydronephrosis was brought to light by the finding of a raised blood urea as part of the investigation of failure to thrive. Of the 5 cases with renal masses 1 was originally thought to be a Wilms' tumour.

Both patients presenting with renal trauma suffered a minor injury, quite disproportionate to the degree of renal trauma—a feature noted by others (Slade, Evans and Roylance, 1961). In 2 patients hydronephrosis was an unexpected finding on urography performed as part of the investigation of enuresis. Further assessment of the 63 patients showed that 4 had an associated congenital heart lesion and in 2 there were similarly unassociated congenital disorders of the hind gut. These 6 patients presented during the first year of life. We excluded from the series 6 newborn infants who died from other conditions, mainly cardiac, who were found at post mortem to have coincidental hydronephrosis.

Diagnosis

Excretion urography was performed in all cases and this examination remains the cornerstone of diagnosis in this condition (Table II). In addition to urography, retrograde ureterography was performed in 10 patients. A renogram in 6 and a renal scan in 1 patient were the only isotope

Read at the 32nd Annual Meeting of the British Association of Urological Surgeons in London, June 1976.

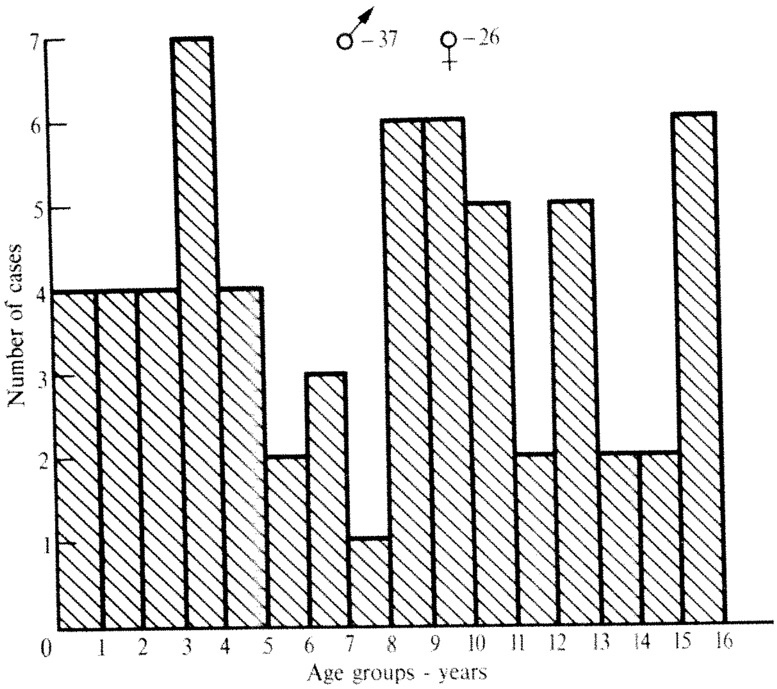


Fig. 1. Hydronephrosis in children. Age when first seen.

studies carried out. Micturating cystography was employed in 2 cases but in neither case was reflux shown. In 14 cases pressure studies involving manometric recording of the renal pelvis were used. The technique and indications for this type of study have been reported elsewhere (Whitaker, 1975).

Aetiology

The aetiology of hydronephrosis remains a contentious subject and it is accepted that retrospective studies of surgeons' operating notes are unlikely to provide much new information. Nevertheless, we have listed (Table III) the operative descriptions of the pelvi-ureteric junction in 50 hydronephrotic kidneys operated upon. In 19 no useful information was available. As in other series stenosis of the junction predominates.

Although a lower pole vessel was found in association with a degree of narrowing of the pelvi-ureteric junction in 14 patients, in only 11 cases was this vessel thought by the surgeon to be the primary cause of the obstruction.

Treatment

In all 63 children an operation was performed and the 69 procedures are outlined in Table IV. In the majority of cases a pyeloplasty was performed, either by the Hynes-Anderson disconnection technique or by the Culp/Scardino flap operation. In 9 cases a pyeloplasty was not performed but the operation was a mobilisation of the upper ureter and pelvi-ureteric junction and displacement of a lower polar vessel which was thought to be the primary cause of the obstruction. In 5 cases the vessel was displaced and buried in a tunnel of renal pelvis, in 3 the

Table I

Symptoms of Hydronephrosis

Loin pain	25
Generalised abdominal pain	9
Haematuria	13
Urinary infection	21
Raised blood urea	3
Mass	5
Trauma	2
Incidental	2

Table II

Diagnostic Techniques

Urogram	63
Urogram and ureterogram	10
Renogram	6
Ultrasound	1
Scan	1
Dynamic studies	14

Table III

Primary cause of Obstruction as described in the Operative Notes

Pelvi-ureteric junction stenosis	36
Lower polar vessel	11
Retrocaval ureter	1
Ureteric fibrosis	2
Not stated	19

Table IV

Operative Techniques

Hynes-Anderson pyeloplasty	27
Hynes-Anderson pyeloplasty plus Nephroplasty	6
Hynes-Anderson pyeloplasty plus pyelolithotomy	1
Culp/Scardino pyeloplasty	13
Culp/Scardino pyeloplasty plus Nephroplasty	2
Lower polar vessel: Mobilisation	5
Division	3
Nephroplasty	1
Ureterotomy	1
Nephrectomy	8
Not recorded	2
Total	69

vessel was divided, and in 1 a nephroplasty alone was performed. A simplified form of nephroplasty was also performed in combination with 6 Hynes-Anderson and 2 Culp/Scardino pyeloplasties. 1 patient had a pyelolithotomy in association with a pyeloplasty and in 1 case an intubated ureterotomy was successfully used to treat a short congenital stricture of the upper ureter.

8 children had a nephrectomy for their hydronephrosis and the indications for these were described as pyonephrosis (1) chronic pyelonephritis (2), thin cortex (2), cystic changes (2) and ureteric stricture (1).

Results

Of the 34 children presenting with either loin pain or generalised abdominal pain 20 were relieved of their pain, 8 had intermittent pain for less than 12 months and then became free, whilst of the remaining 6 patients the pain persisted after the 12-month period. Of these patients with persistent pain, urography showed a poorly excreting kidney in 1 child with persistent urinary tract infection and non-excretion in another. Both these kidneys have now been removed. In a further 2 children with persistent pain the kidney was re-explored and an inter-operative pressure/flow study performed on the renal pelvis. In each patient it revealed no evidence of residual obstruction and the kidneys have been preserved. It was found in both these children that the muscle cutting incision had originally been repaired with nylon. It was replaced by catgut and early follow-up of these 2 children shows an encouraging lessening of the pain. It may well be that the growing child can experience discomfort from unyielding nylon.

In the 21 cases who presented with infection, 9 were cured by operation but in the remainder troublesome urinary sepsis, as defined by more than 3 attacks of proven infection in 12 months, persisted. Follow-up urograms in these children with persistent postoperative urinary infections reveal considerable stasis even though there was no residual obstruction, and in 1 there was a secondary infective stone in the renal pelvis.

Though urologists are well aware of the often disappointing appearances of post-pyeloplasty urograms, excretion urography remains the simplest objective assessment. These postoperative urograms were assessed using the criteria of improved excretion, reduction in calyceal dilatation and improvement in ureteric filling. In this way follow-up urograms, performed on average 6 months after surgery, were described as excellent, good or poor. In 15 cases there was inadequate information but the overall results of the remaining 54 cases are shown in Table V.

Finally, each group of X-ray results was compared with the type of operation used. The results are shown in Table V. The best results in this series were obtained with the Hynes-Anderson pyeloplasty and included in these were those pyeloplasties combined with a nephroplasty.

Discussion

Loin pain, as in other series (Nixon, 1953; Roberts and Slade, 1964) remains the commonest presenting symptom. Some children were unable to localise their pain and generalised abdominal discomfort was the feature in many. Haematuria was not uncommon and probably is due to rupture of veins in the pelvis secondary to distension or, as suggested by Deming (1951) it may originate in the distal tubule. Urinary sepsis was a common feature in this series and seems more common in children than in the "all ages" study (Roberts and Slade, 1964).

Retrograde ureterography was used in 10 patients, 3 of whom had a non-excreting kidney on urography. This investigation is not without risk of infection and pyonephrosis and should be reserved for cases where the diagnosis is in doubt. Reflux induced hydronephrosis is, however, a definite entity (Whitaker, 1976) and a cystogram should be performed in a child with a wide ureter in association with a hydronephrosis.

Quantitative renography has been suggested for the postoperative assessment of hydronephrosis (Kathel, 1972) but we have not found it a useful tool in the diagnosis of difficult cases of obstruction.

A percutaneous or inter-operative pressure/flow study has proved to be a most valuable investigation in the equivocal case and gives an objective assessment of the symptoms and urographic findings. If the pelvis can tolerate a flow of 10 ml/minute at not greater pressure drop between the pelvis and bladder than 12 cm water, it is not obstructed and probably does not require surgery (Whitaker, 1976*a*).

This retrospective study has not significantly advanced our knowledge of the aetiology of hydronephrosis and in particular the place of the lower polar vessel as an obstructive factor remains uncertain. It seems in this series that in 11 patients the vessel was the primary cause of the obstruction but we accept that without dynamic assessment this remains unsubstantiated. There seems little doubt that the vessels can worsen an obstruction that is already present, probably by the mechanism so clearly described by Robinson (1959) of herniation of the pelvis through the vascular foramen. After dynamic studies one of us (R. H. W.) feels that the vessels are rarely, if ever, the primary cause of obstruction. In this series, as in others (Nixon, 1953; Hanley, 1959; Roberts and Slade, 1964; Smith, 1972) we found a high incidence of lower polar vessels. This discussion is complicated by the fact that occasionally good results are recorded in the management of hydronephrosis by operative procedures which do not involve formal reconstruction of the pelvi-ureteric junction. It is, however, stressed that where the displacement of a lower polar vessel is contemplated this must be combined with an extensive dissection of the kinked pelvi-ureteric junction so as to remove any so-called adhesions.

Table V

Radiological Results compared with the Operation Performed

	Excellent	Good	Poor	Non-excreting
Hynes-Anderson	9	11	3	–
Hynes-Anderson plus nephroplasty	5	1	–	–
Culp/Scardino	2	7	2	1
Culp/Scardino plus nephroplasty	1	1	–	–
Vessel mobilisation	3	3	–	–
Vessel division	–	–	3	–
Nephroplasty	1	–	–	–
Intubated ureterotomy	–	1	–	–
Total	21	24	8	1

Pain persisting after a pyeloplasty may arise in the incision, particularly in a child if the muscle layers have been repaired with nylon. Where doubt exists about the possibility of any residual obstruction dynamic studies of the renal pelvis are the investigation of choice.

In this series it would seem that relief of sepsis is not guaranteed by pyeloplasty and this is usually because it is impossible to remove all the "sump" of residual urine in the intrarenal portion of the pelvis.

Despite its limitation the urogram remains the most useful and simplest method of post-operative assessment.

Hynes-Anderson pyeloplasty was the commonest operation (Table V). As well as reflecting the personal preference of many urologists it is also an operation which allows transposition of a lower polar vessel at the same time as the pyeloplasty. Although encouraging results have been obtained by displacement of the vessels alone we feel it is advisable to perform also a pyeloplasty unless dynamic studies suggest that it is unnecessary.

In this series the best results were obtained with the Hynes-Anderson pyeloplasty. This was also the case in the more gross examples of hydronephrosis with marked intra-renal dilatation provided the pyeloplasty was combined with a nephroplasty. Nephroplasty, an operation originally designed for the displacement of lower polar vessels, can be readily combined with a pyeloplasty and technically has been simplified to a mere sewing together of the upper and lower poles of the kidney. This can best be achieved on a kidney with a thin cortex and dilated calyces—a happy coincidence since this is precisely the situation which will benefit from nephroplasty, where the aim is a reduction in intra-renal dilatation and the encouragement of dependant drainage. Greater awareness of the possibility of combining nephroplasty with pyeloplasty might well have reduced the incidence of primary nephrectomy in this series.

Summary

A retrospective review of 63 children with primary pelvic hydronephrosis has revealed many features similar to those in adults.

A plea is made for the greater use of pressure/flow studies in the renal pelvis in the assessment of hydronephrosis.

The value of a modified and simplified nephroplasty as an adjunct to pyeloplasty in the more advanced obstructive cases is described and its greater use encouraged.

References

DEMING, C. L. (1951). Effects of intrarenal hydronephrosis on the components of the renal cortex. *Journal of Urology*, **65**, 748-753.

HANLEY, H. G. (1959). The pelviureteric junction: a cinepyelography study. *British Journal of Urology*, **31**, 377-384.

KATHEL, B. L. (1972). Quantitation of the isotope renogram by analogue computer simulation. In *Problems in Paediatric Urology*, ed. J. H. Johnston and R. J. Scholtmeijer. Amsterdam: Excerpta Medica, pp. 257-270.

NIXON, H. H. (1953). Hydronephrosis in children—a clinical study of 78 cases with special reference to the role of aberrant renal vessels and the results of conservative operations. *British Journal of Surgery*, **40**, 601-609.

ROBERTS, J. B. M. and SLADE, N. (1964). The natural history of primary pelvic hydronephrosis. *British Journal of Surgery*, **51**, 759-762.

ROBINSON, R. H. O. B. (1959). Hydronephrosis. *British Journal of Urology*, **31**, 385-390.

SLADE, N., EVANS, K. T. and ROYLANCE, J. (1961). The late results of closed renal injuries. *British Journal of Surgery*, **49**, 194-197.

SMITH, P. J. B. (1972). Hamilton Stewart nephroplasty. *Proceedings of the Royal Society of Medicine*, **65**, 1022-1023.

WHITAKER, R. H. (1975). Equivocal pelviureteric obstruction. *British Journal of Urology*, **47**, 771-779.

WHITAKER, R. H. (1976). Reflux induced pelvi-ureteric obstruction. *British Journal of Urology*, **48**, 555-560.

The Authors

Patrick Smith, FRCS, Consultant Urologist, St. Martin's Hospital, Bath.
Michael Roberts, FRCS, Consultant Urologist, Bristol Royal Infirmary.
Robert H. Whitaker, FRCS, Consultant Urologist, Addenbrooke's Hospital, Cambridge.
Abdel Raouf Garousche, FRCSE, Senior House Officer in Urology, Bristol Royal Infirmary.

British Journal of Urology (1976), **48**, 555-560 ©

Reflux Induced Pelvi-ureteric Obstruction

ROBERT H. WHITAKER
Department of Urology, Addenbrooke's Hospital, Cambridge

The purpose of this paper is to consider the pelvi-ureteric obstruction which is occasionally seen in association with vesico-ureteric reflux in the light of recent and more critical reappraisal of hydronephrosis (Whitaker, 1975, 1976).

With the advent of image intensification and good quality micturition cystourethrography it was soon recognised that a marked degree of reflux could result in an appearance of the renal pelvis suggestive of pelvi-ureteric obstruction (Gross and Sanderson, 1961; Hutch, Hinman and Miller, 1962). In these early descriptions it was not stated how long the pelvis remained full after voiding was completed so that no real evidence of an obstruction was presented. However, Hutch *et al.* (1962) did suggest that in the presence of a closed type of renal pelvis (Hanley, 1959) reflux could induce a hydronephrosis which remains, and perhaps even becomes symptomatic, long after the reflux has spontaneously stopped.

Shopfner (1966) made the important observation, sadly all too often forgotten, that not all dilated renal pelves, with or without reflux, are obstructed. But he agreed that reflux, perhaps with infection, could play a major role in the pathogenesis of pelvi-ureteric obstruction. He stressed the need to see how quickly the pelvis empties after voiding in determining whether or not a meaningful obstruction is present.

Smith (1970) from his own experience and a review of the literature states that the pelvi-ureteric obstruction seen with reflux is usually secondary to the ureteric changes that accompany reflux. He does concede, however, that the pelvi-ureteric obstruction could be a primary abnormality of the idiopathic type and the reflux incidental as both conditions occur in a similar age-group.

Williams (1974) accepts 2 distinct groups. 1 with pelvi-ureteric obstruction which presents as a renal problem and needs a pyeloplasty. The reflux which is incidental and irrelevant to the aetiology of the hydronephrosis may stop spontaneously after the pyeloplasty. A second group develop hydronephrosis, which may become obstructed, as a result of massive reflux into the pelvis. At operation there is a secondary kinking at the pelvi-ureteric junction with some narrowing but the exact site of hold up is not altogether obvious. In this latter group the pelvis balloons during micturition and remains full. Williams suggests that this is due to atonicity of the pelvic musculature. This phenomenon can disappear after reflux prevention when the pelvi-ureteric junction is called upon to cope only with the normal downward urine load and he believes that the findings of this type of pelvis is a relative indication for reflux prevention.

Johnston (1976) suggests that the aetiology of the obstruction is the sudden gross filling of the renal pelvis with refluxed urine which leads to an increased pelvi-ureteric angulation and subsequent severe pelvic distension and delayed emptying.

Thus it is clear that although descriptions of this condition abound, few if any attempts have been made to define at what stage such a reflux induced hydronephrosis has a significant degree of obstruction and needs surgical attention; the term obstruction is often loosely used. Shopfner (1966) could see that the answer lay in dynamic assessment and attempted to analyse obstruction

Read at the 32nd Annual Meeting of the British Association of Urological Surgeons in London, June 1976.

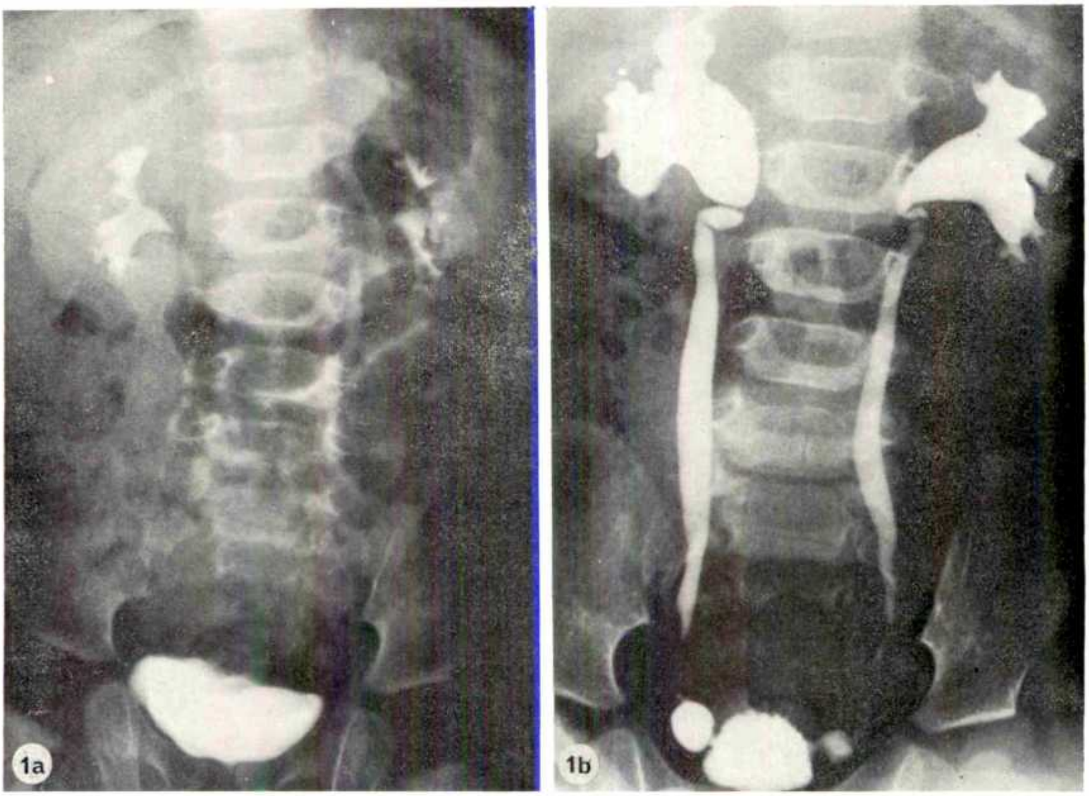


Fig. 1. 1-year-old boy with recurrent urinary tract infections. A, Urogram with no suspicion of hydronephrosis. B, Micturating cystogram showing gross reflux with pelvic distension suggesting possible secondary pelvi-ureteric obstruction particularly on the right. However, both pelves drained readily after micturition.

on these lines but found the results sufficiently variable to be of no convincing value. Hutch and Tanagho (1965) discussed the theoretical aspects of the dynamics of this type of obstruction but did not put their theories to practical or clinical use.

Objectives

The sometimes remarkable contrast between the appearances of the renal pelvis and the calyces in the urogram and the micturating cystogram may lead one to suspect too easily an element of pelvi-ureteric obstruction where none exists (Fig. 1). The objective was to assess the best means of diagnosing a true obstruction secondary to reflux.

Clinical Studies

During micturating cystography in patients who show reflux we watch carefully to see how long the renal pelvis remains full and have been surprised how readily the most grossly distended pelvis can empty after voiding has ceased. In the few that have remained a little full we have found it difficult to assess the significance because of several variable factors which include the degree of dehydration and the position and co-operation of the patient.

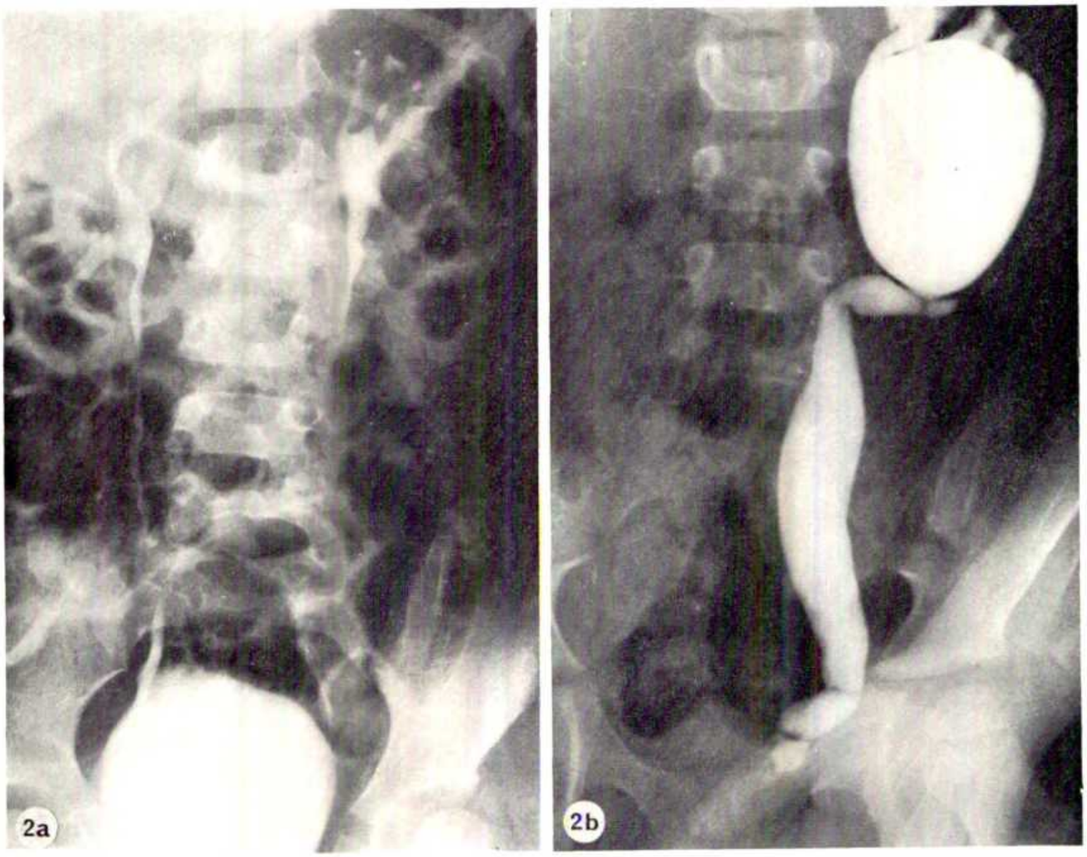


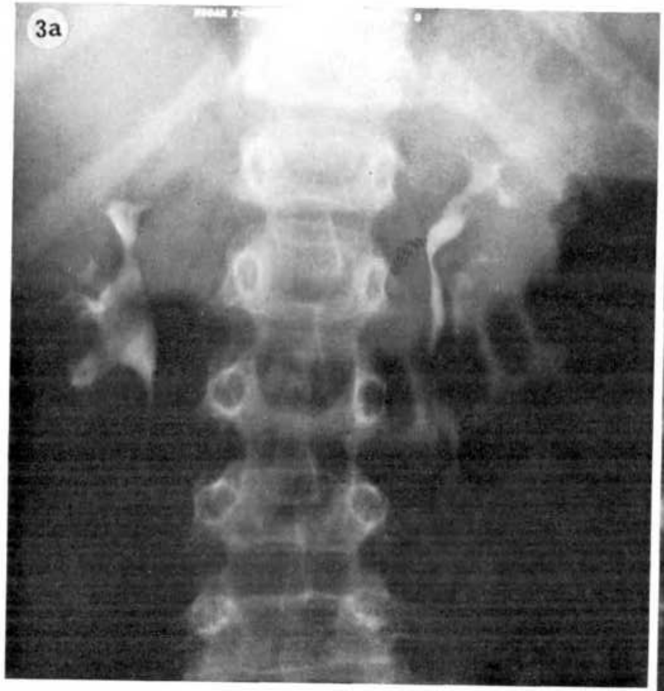
Fig. 2. A, Urogram and, B, Micturating cystogram of a 5-year-old boy with urinary tract infection and bouts of left loin pain. There is a gross discrepancy between the 2 appearances. After micturition the left renal pelvis remained full after the ureter had emptied. After a left ureteric re-implantation he has had no further pain and the follow-up urogram shows no pelvic dilatation.

The patients of particular interest are those with no suggestion on the urogram of a hydronephrosis but who have marked pelvic dilatation on voiding. In other words, patients in whom there is no suggestion of a primary pelvi-ureteric obstruction.

The degree of pelvic dilatation and appearances suggestive of obstruction are variable even in the same patient. Figure 1 shows the urogram and cystogram of a young boy with repeated urinary infections. The right side is more suggestive of a secondary pelvi-ureteric obstruction but in fact both emptied readily after voiding. Figure 2 shows a boy with a similar history but his renal pelvis took several minutes to empty and this was a factor that influenced our decision in this child to re-implant his ureter.

Figure 3, A shows the urogram of a child in whom detailed studies were possible. It shows a small scarred, dysplastic lower pole of a duplex left kidney. There is no suggestion on this urogram of a primary pelvi-ureteric obstruction. On filling his bladder with contrast medium it ran freely up into this lower pole pelvis (Fig. 3, B). On voiding, the pelvis rapidly fills and in this boy it remained full for the several minutes that it took to complete this study (Fig. 3, C).

Because he had such a poor lower pole a partial nephroureterectomy was undertaken and at the time of operation the pelvi-ureteric junction was studied. Because our pressure/flow apparatus



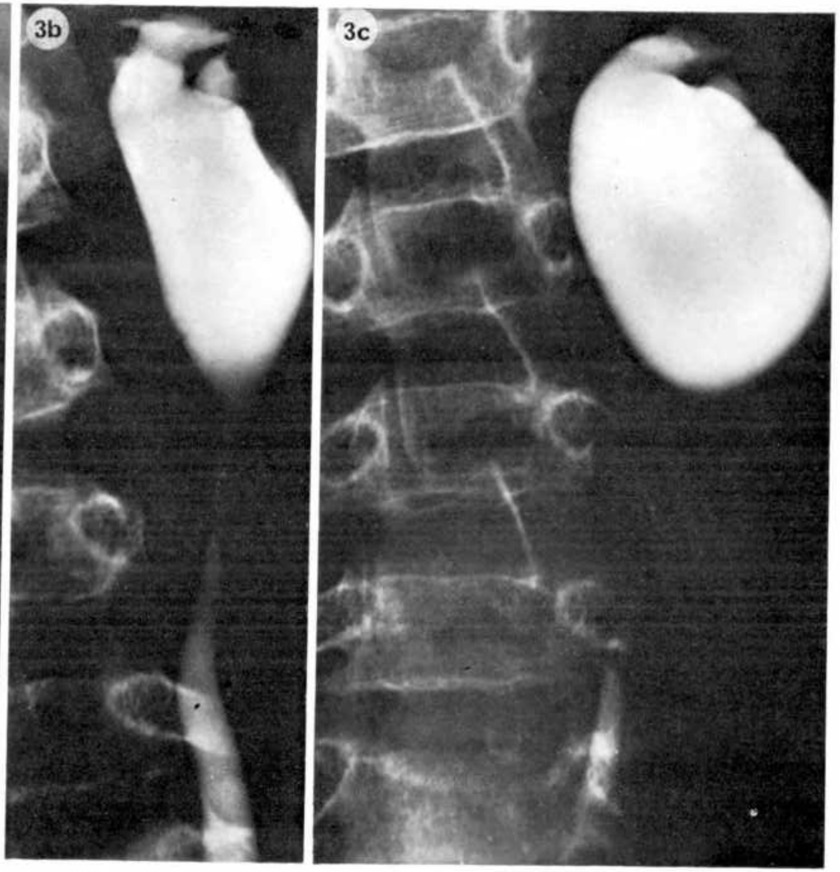


Fig. 3. A 9-year-old boy with an 8-month history of left sided pain and urinary tract infection. He had reflux into a small scarred lower pole of the duplex left kidney. A, Urogram. Poor excretion but no suggestion of a hydronephrosis. B, During bladder filling there is partial distension of the left renal pelvis. C, Just after finishing voiding. The pelvis remained full for several minutes even with the patient standing.

was not available at that time a syringe filled with saline was used to fill the system. The needle was inserted into the lumen of the ureter 3 inches below the pelvi-ureteric junction with the ureter temporarily occluded below that level. The pelvis was initially flaccid but filled and became rounded as the saline was injected. When the pelvis was tense the syringe was removed and the ureter released. The pelvis remained full and tense and the pelvi-ureteric junction would conduct no fluid even when the pelvis was squeezed. The situation now had the typical features of an idiopathic type of pelvi-ureteric obstruction. A partial nephroureterectomy was then completed.

Discussion

Atonicity (Williams, 1974) and acute angulation (Johnston, 1976) may well play a part in the production of this phenomenon but in the truly obstructed pelvis further factors are probably involved. It is clear that the easy distensibility of the pelvis in these cases converts a funnel-shaped pelvi-ureteric junction into a shape not unlike a plug-hole in a bath. The downward propagating pelvic contraction wave can no longer form a bolus but having failed to do so the circular component contracts at the first point of occlusion and this action actively obstructs the lumen.

The implication here is that this is an active, as opposed to passive, obstructive phenomenon and akin to that seen in the idiopathic form of pelvi-ureteric obstruction (Whitaker, 1975).

As others have suggested (Hutch *et al.*, 1962) some renal pelves are more susceptible to becoming obstructed in the presence of reflux but whether the defect is primary or secondary to the reflux is largely an academic argument. As far as treatment is concerned, and particularly if pyeloplasty is being considered, it is essential to decide whether or not a significant degree of true obstruction is present. More evidence is needed than a full pelvis at the height of voiding. Considerably delayed emptying is suggestive of obstruction but this is a situation in which a pressure/flow perfusion study, performed percutaneously under radiographic control, could supply the absolute evidence of obstruction that is needed.

In the group with urographic appearances suggestive of a pelvi-ureteric obstruction the diagnosis of obstruction must first be confirmed and a pyeloplasty performed. In the second group where there is so often a severe dysplasia or renal reduplication but the urogram shows no hydronephrosis, the choice of treatment is a re-implantation of the ureter or a partial or total nephroureterectomy. A pyeloplasty will only be necessary in this group if the diagnosis of obstruction is substantiated after a re-implantation.

Finally, it is of interest to speculate whether the occasional patient with a large renal pelvis a little suggestive of pelvi-ureteric obstruction but with a wide ureter below it and *no reflux* may have had spontaneous cessation of reflux and this is the aftermath. This would be an explanation for the non-obstructed hydronephrosis which undoubtably exists (Shopfner, 1966; Whitaker, 1975).

Summary

The phenomenon of pelvi-ureteric obstruction which is induced by vesico-ureteric reflux is well documented but ill understood. The radiographic findings can be impressive to an extent that obstruction is probably often over-diagnosed.

Before considering a pyeloplasty it is essential to confirm the true obstructive nature of the problem.

Where the urogram is not suggestive of an obstruction a re-implantation of the ureter will usually stop the gross pelvic dilatation.

It is suggested that the obstruction is at least partially an active process.

References

GROSS, K. E. and SANDERSON, S. S. (1961). Cineurethrography and voiding cinecystography with special attention to vesico-ureteral reflux. *Radiology*, **77**, 573-585.

HANLEY, H. G. (1959). The pelvi-ureteric junction: a cinepyelography study. *British Journal of Urology*, **31**, 377-384.

HUTCH, J. A., HINMAN, F. and MILLER, E. R. (1962). Reflux as a cause of hydronephrosis and chronic pyelonephritis. *Journal of Urology*, **88**, 169-175.

HUTCH, J. A. and TANAGHO, E. A. (1965). Etiology of non-occlusive ureteral dilatation. *Journal of Urology*, **93**, 177-184.

JOHNSTON, J. H. (1976). In *Urology*, ed. J. P. Blandy. Oxford: Blackwell, p. 545.

SHOPFNER, C. E. (1966). Ureteropelvic junction obstruction. *American Journal of Roentgenology and Radium Therapy*, **98**, 148-159.

SMITH, D. R. (1970). In *Urology*, ed. M. F. Campbell and J. H. Harrison, 3rd ed. Philadelphia: Saunders, vol. 1, pp. 365 and 366.

WHITAKER, R. H. (1975). Some observations and theories on the wide ureter and hydronephrosis. *British Journal of Urology*, **47**, 377-385.

WHITAKER, R. H. (1975). Equivocal pelviureteric obstruction. *British Journal of Urology*, **47**, 771-779.

WILLIAMS, D. I. (1974). In *Encyclopedia of Urology*, XV Supplement. Berlin: Springer, pp. 119 and 125.

The Author

Robert H. Whitaker, MChir, FRCS, Consultant Urologist.

Requests for reprints to the author at Addenbrooke's Hospital, Cambridge.

British Journal of Urology (1976), **48**, 561–566 ©

Occupational Bladder Tumour Cases Identified During Ten Years' Interviewing of Patients

JOAN M. DAVIES, SHEENA M. SOMERVILLE and D. M. WALLACE
Institute of Cancer Research and Royal Marsden Hospital, London

It has been recognised for many years that a proportion of patients with bladder cancer have their tumours caused by past exposure at work to carcinogenic aromatic amines. This aspect of the disease is well documented, and has recently been reviewed by Kipling (1976).

All patients attending the Royal Marsden Hospital (R.M.H.) with urothelial tumours are routinely interviewed, and full occupational histories are taken. One use of the histories collected has been to identify patients with occupational tumours who are covered by the definition of urothelial cancer as a Prescribed Industrial Disease (P.I.D.), and we describe our experience of such cases over the last 10 years.

Bladder cancer was first added to the list of Prescribed Industrial Diseases in 1953, and the prescription now covers the following sites:

> No. 39. "Primary neoplasm of the epithelial lining of the urinary bladder (Papilloma of the bladder), or . . . of the renal pelvis or . . . of the ureter or . . . of the urethra."

For convenience, the term "bladder tumour" is used in this paper. The description "papilloma of the bladder" is used in P.I.D. claims to spare patients from seeing their illness referred to as "cancer".

A man or woman who develops a bladder tumour and who has been exposed at work to one of the urinary tract carcinogens covered by the Prescription can claim "benefit" from the Department of Health and Social Security (D.H.S.S.) in the form of a tax-free pension or gratuity; if a man dies from industrial disease his widow receives a slightly higher state pension. Retired patients are eligible in the same way as those still at work.

Patients and Interviews

About 100 new patients come to the R.M.H. each year with urothelial tumours, and this paper deals with the 1,000 patients attending during just over 10 years up to the end of 1975. Some three-quarters of the patients were men, and the majority were in their 60s and 70s (Table I). Although new to the R.M.H. many of these cases had been first diagnosed or treated at other hospitals in the London area.

These 1,000 patients were asked about all their jobs since leaving school. They were also asked whether they had ever done certain kinds of work—work with rubber, for example—as a check in case a relevant job had been forgotten, or in case some job had an important aspect that had not been mentioned. In addition they were asked specifically what work they did during the Second World War, when men may have worked on different products, and some women did factory work for the only time in their lives. In general exposure to recognised urinary carcinogens is a risk of the past, and we were much more interested in what jobs the patients had been doing 20 or more years previously than in their current jobs.

Read at the 32nd Annual Meeting of the British Association of Urological Surgeons in London, June 1976.

Table I

Number of R.M.H. Bladder Tumour Patients Interviewed

Ages	Men	Women	Total
Under 40	5	4	9
40-49	35	17	52
50-59	154	39	193
60-69	329	73	402
70-79	216	78	294
80 and over	36	14	50
All ages	775	225	1000

The prescription of bladder cancer as an industrial disease specifies the nature of the occupation which may make a patient eligible as follows:

Any occupation involving

(*a*) Work in a building in which any of the following substances is produced for commercial purposes:
  (i) Alpha-naphthylamine or beta-naphthylamine.
  (ii) Diphenyl substituted by at least one nitro or primary amino group or by at least one nitro and primary amino group.
  (iii) Any of the substances mentioned in sub-paragraph (ii) above if further ring substituted by halogeno, methyl or methoxy groups, but not by other groups.
  (iv) The salts of any of the substances mentioned in sub-paragraphs (i) to (iii) above.
  (v) Auramine or magenta;

(*b*) the use or handling of any of the substances mentioned in sub-paragraphs (i) to (iv) of paragraph (*a*), or work in a process in which any such substance is used or handled or is liberated;

(*c*) the maintenance or cleaning of any plant or machinery used in any such process as is mentioned in paragraph (*b*), or the cleaning of clothing used in any such building as is mentioned in paragraph (*a*) if such clothing is cleaned within the works of which the building forms a part or in a laundry maintained and used solely in connection with such works.

Translating this prescription into terms of particular occupations, we were looking for patients exposed to the carcinogenic aromatic amines (principally alpha-naphthylamine, beta-naphthylamine and benzidine) in factories manufacturing dyestuffs or pigments, other types of chemical factories or textile printing firms where these chemicals were used, rubber or electric cable factories, the retort houses of gasworks, for rat catchers who used the rodenticide "Antu" (which contained alpha-naphthylamine), and for chemists or laboratory technicians who had used the carcinogens in routine testing. But in order to identify patients with *definite* exposure to carcinogens it was necessary to note and examine the histories of a broader group: all those where there was a *possibility* of risk; this in practice included all patients reporting any work connected with chemicals, rubber, cables or gasworks. In most cases patients themselves have no idea of the possible significance of their past jobs.

Table II

Number of Patients with Work Histories Indicating Possible Exposure to Bladder Carcinogens

Ages	Patients interviewed	Patients with possible exposure	
Under 40	9	0	—
40-49	52	7	14%
50-59	193	31	16%
60-69	402	40	10%
70-79	294	24	8%
80 and over	50	2	4%
All ages	1000	104	10%

86 men, all ages: 11%. 18 women, all ages: 8%.

Table III

Relevant Occupations of Patients with Possible Exposure to Bladder Carcinogens

Occupation	Men	Women	Total
Rubber	36	8	44
Cables	15	7	22
Gasworks	25	1	26
Miscellaneous*	10	2	12
Total	86	18	104

* Dyestuff and paint manufacture, chemical factories, laboratories, rat poisons.

Results

Overall 10% of patients gave histories which suggested possible risks, but the proportion was higher in the younger age-groups (Table II).

The distribution of relevant occupations with possible exposure to risk, is probably typical for patients in London, which is a centre of the cable industry and to a lesser extent of the rubber industry, but the picture would differ in other parts of the country (Table III). The many cases of occupational cancer connected with the manufacture of dyestuffs belong mainly to the north of England; towns where rubber workers might predominate include Birmingham, Stoke-on-Trent, Leicester and Liverpool among others. In contrast, gasworks producing coal-gas used to be found all over the country.

From among the patients with possible contact with carcinogens it was then necessary to distinguish those with histories of exposure definite enough for them to be eligible to claim P.I.D. benefit. This distinction is not always easy, but it is important, for if a patient is eligible this must be acted on, but it is unfortunate if patients are advised that their illness is occupational when this cannot be substantiated: they may then go to considerable trouble to submit claims which are later rejected, and may be left with a needless sense of grievance.

The total number of patients considered eligible for P.I.D. benefit was 37; for all patients interviewed the proportions were 5% of men and 1% of women (Table IV).

Rubber and Cable Workers

For rubber and cable workers it must be borne in mind that their risk arose from the past use of rubber additives, mainly the anti-oxidant "Nonox S", which contained small amounts of uncombined naphthylamines (Case and Hosker, 1954; Davies, 1965). This anti-oxidant was used in most rubber and electric cable factories from the late 1920s until 1949, when it was withdrawn because its danger was realised. The risk was greatest for workers employed in rubber processing departments, but the hazard from dust and fumes extended to men or women who worked in adjacent shops or who had occasion to go into the processing departments—perhaps to do cleaning or maintenance work, or in a supervisory capacity, or merely on their way in and out of their own departments.

Table IV

Number of Patients Eligible for P.I.D. Benefit, by Relevant Occupation

Occupation	Number with possible exposure	Number eligible Men	Women	Total
Rubber	44	16	1	17
Cables	22	6	1	7
Gasworks	26	10	0	10
Miscellaneous	12	3	0	3
Total	104	35	2	37

24 workers were considered eligible to claim P.I.D. benefit, and 42 cases were rejected on the following grounds:

8 patients had worked in rubber or cable factories but had left before the introduction of "Nonox S", and 11 men and women had started work only after its withdrawal in 1949.

2 men had been employed at rubber factories for only 1 to 3 weeks, and could remember nothing about these jobs; 1 woman could not recall which cable factory she had worked at during the war, nor any details of this job.

6 former employees at large cable factories had not worked anywhere near the rubber processing departments, but in separate buildings.

The remaining 14 patients had had some rubber contact which appeared to us too slight for claims to be feasible; for example, 1 patient was a fireman who had fought 3 large fires at rubber factories or warehouses, and 2 were engineers who had visited rubber factories occasionally on contract work.

Some of the 24 eligible patients from rubber or cable work would have been very hard to overlook, since they were still employed in these industries when their tumours were diagnosed. But in some other cases the relevant job was brief and appeared remote to the patients. For example, a 52-year-old man interviewed in 1973 had been a lift mechanic for many years, but for some months during 1936-37 he had worked at a small rubber factory in Middlesex. Another patient was a building labourer, but had worked briefly during the war at a tyre factory in Gravesend. Short jobs like these can easily be overlooked unless patients are asked very specifically whether they have ever worked with rubber or cables.

To make matters more difficult, the factories involved in these last 2 instances had since closed down, although in 1 case the parent company was still operating. This is a not infrequent problem, and means that it may not be possible to check whether the firm in question used "Nonox S". Advice as to whether work at the relevant factory would have involved exposure to carcinogens might be obtainable from Dr H. G. Parkes of the Health Research Unit of the British Rubber Manufacturers' Association in Birmingham, in these or other cases where the urologist is unsure whether to advise his patient to submit a claim.

Gasworkers

In the case of gasworkers, Doll *et al.* (1965, 1972) have shown that retort house workers suffer excess mortality from bladder cancer, and beta-naphthylamine has been shown to be present in the air of retort houses. Patients who had been gasworkers were considered to be eligible for

P.I.D. benefit if they had been employed specifically in the retort houses of gasworks or had done jobs which took them there regularly.

On these criteria 10 patients who had been gasworkers were eligible. 4 men had worked for between 18 and 37 years entirely in retort houses; another 4 had been employed at gasworks for between 16 and 45 years, and had either worked for part of this time exclusively in the retort houses, or had had jobs as fitters which involved spending regular periods of time there. 2 other cases were borderline: 1 man reported doing retort house work for 10-12 months in 1947, and the other went daily into the retort house in the course of repair work from 1961 to 1966, a relatively short time before he developed his tumour in 1968.

The other 16 former gasworkers were not advised to submit claims. 2 of these had worked at gasworks abroad before coming to England, and would therefore have been ineligible. 5 men reported rather brief spells of work in retort houses, in 2 cases as long ago as 1912 and 1917; 5 others went there only occasionally in the course of relatively short periods of employment at gasworks. 3 other men had not worked anywhere near the retort houses, and 1 man could not remember when or at which gasworks he had been employed.

Miscellaneous Workers

3 of these 12 patients appeared eligible, and made successful claims for P.I.D. benefit. 1 was an analytical chemist who in the past had for some years used small amounts of the carcinogens in routine testing of food and water for certain contaminants. Another man, aged 47 at interview, was a laboratory technician who for many years until the late 1960s had made very frequent use of ortho-tolidine for testing the chlorine content of water. The 3rd patient had worked for a firm of paint manufacturers since the 1920s, and in early years this firm had compounded their own dry colours, and were known to have used benzidine.

The other 9 patients in this group did not appear on examination to have had contact with recognised carcinogens. Some had worked at chemical factories, but the products manufactured by the firms would not have involved the use of the recognised carcinogens; in other cases the patients' work would not have taken them near processes involving any risk—1 man, for example, was a commercial traveller before the war for a northern firm of dyestuff manufacturers, but he never went into the works. Another patient had earlier been a rat catcher, but had never used "Antu".

Discussion

In this paper it is explained which bladder tumour patients were advised to claim P.I.D. benefit; the practical aspects of these claims as they concern the clinician will be presented elsewhere.

All our patients who submitted claims had these accepted, and received amounts of benefit varying according to their degree of disablement as assessed by D.H.S.S. medical boards. For example, 1 patient who remained tumour-free following a single cystoscopic resection was assessed at 10%; at current rates a 10% assessment carries a yearly gratuity of £130. Another patient was assessed at 40% following a partial cystectomy and radiotherapy; he receives a weekly pension of £10. For a patient who underwent a total cystectomy the assessment was 80%, and he receives £20 per week. Most patients are periodically re-assessed, and if their disease progresses they receive higher rates of benefit; the maximum weekly rate is £25 for an assessment of 100%.

Quite separately from their receipt of P.I.D. benefit from the D.H.S.S., some patients may obtain ex-gratia payments or legal compensation from industry. Those who were exposed to risk at rubber or cable factories after about 1942 (or their widows) may be able to obtain out-of-court settlements from the manufacturers of "Nonox S". The amounts awarded vary considerably in individual cases, and take into account the patient's age, type and duration of treatment and prognosis. The smallest settlement we have encountered is £2,000 (received by a widow), but a figure of around £8,000 is more usual.

It can readily be seen that patients' circumstances may be eased considerably by these pensions or settlements.

Summary

All patients attending the Royal Marsden Hospital with urothelial tumours have their occupational histories taken.

About 10% of histories suggest a possibility of past exposure to urinary carcinogens, and on examination 4% indicate definite exposures justifying claims for Prescribed Industrial Disease benefit.

References

CASE, R. A. M. and HOSKER, M. E. (1954). Tumour of the urinary bladder as an occupational disease in the rubber industry in England and Wales. *British Journal of Preventive and Social Medicine*, **8**, 39-50.

DAVIES, J. M. (1965). Bladder tumours in the electric-cable industry. *Lancet*, **ii**, 143-146.

DOLL, R., FISHER, R. E. W., GAMMON, E. J., GUNN, W., HUGHES, G. O., TYRER, F. H. and WILSON, W. (1965). Mortality of gasworkers with special reference to cancers of the lung and bladder, chronic bronchitis, and pneumoconiosis. *British Journal of Industrial Medicine*, **22**, 1-12.

DOLL, R., VESSEY, M. P., BEASLEY, R. W. R., BUCKLEY, A. R., FEAR, E. C., FISHER, R. E. W., GAMMON, E. J., GUNN, W., HUGHES, G. O., LEE, K. and NORMAN-SMITH, B. (1972). Mortality of gasworkers—final report of a prospective study. *British Journal of Industrial Medicine*, **29**, 394-406.

KIPLING, M. D. (1976). Occupational considerations in carcinoma of the urogenital tract. *British Journal of Hospital Medicine*, **15**, 465-472.

The Authors

Joan M. Davies, PhD, Member of the Scientific Staff, Division of Epidemiology, Institute of Cancer Research.
Sheena M. Somerville, BSc, Research Worker, Royal Marsden Hospital.
D. M. Wallace, OBE, MS, FRCS, Emeritus Consultant Urologist, St Peter's Hospitals and Royal Marsden Hospital (now Professor of Urology, University of Riyadh, Saudi Arabia).

Requests for reprints should be sent to Dr J. M. Davies, Institute of Cancer Research, Fulham Road, London SW3 6JB.

British Journal of Urology (1976), **48**, 567–577 ©

Inverted Papilloma of the Lower Urinary Tract

KATHARINE M. CAMERON and CHARLES H. LUPTON
Institute of Urology and Department of Pathology, St Peter's Hospitals, London

The classical "inverted papilloma" is a polypoidal tumour of distinctive histological appearance. It occurs mainly in males and in the region of the trigone, bladder neck or posterior urethra. The lesion appears to behave in a benign fashion and must, therefore, be distinguished from the more common tumours of transitional epithelium.

The name "inverted papilloma" was first used by Potts and Hirst who described a single case in 1963; 10 years later they presented 8 more examples at the 16th Congress of the International Society of Urology in Amsterdam. Altogether 35 other cases have been reported under this name in the English language literature (Table I), and several apparently identical lesions have been described under a variety of different titles (*e.g.* Salm, 1967, case 3). The largest series is that of De Meester, Farrow and Utz (1975) who noted that 4 inverted papillomas had been reported much earlier in the German literature by Paschkis (1927) as "adenoma-like polyps" of the bladder. They are described also in the most recent AFIP fascicle on tumours of the urinary bladder (Koss, 1975).

This benign urothelial lesion has been recognised in this laboratory for some years. In this paper 35 typical cases are presented and the differential diagnosis of other epithelial lesions of the bladder which are also "inverted" is discussed. The series consists of 18 patients investigated at St Peter's Hospitals (Group I) and 17 cases referred for histological opinion (Group II). Sex, age, site and follow-up data have been obtained for the majority of patients in both groups; full clinical details are available only in Group I.

Clinical Features

Of the 35 patients only 2 were females. The ages ranged from 22 to 78 years, with a peak incidence in the 6th and 7th decades.

The most common presenting symptom in Group I was haematuria (Table II) which occurred in 13 patients, 3 of whom also gave a history of recent infection; this was urinary in 2 cases and epididymal in 1 and all 3 had already received treatment when first seen in hospital. 3 of the patients with haematuria also had a degree of bladder outflow obstruction. Obstructive symptoms were present altogether in 7 men, being the sole symptom in 4, but how much they were due to the tumours in the older age-group is difficult to say. 1 patient complained only of penile soreness following the passage of a stone.

Intravenous urography, performed on 13 of the 18 patients, showed normal upper tracts in 10. The abnormal findings were a ureteric calculus, unilateral pyelonephritis and an enlarged kidney of uncertain aetiology in one instance each.

Midstream urine specimens taken on the first visit in 16 patients proved to be sterile in 15. In 1 of the cases with a history of urinary infection *E. coli* was isolated but the organisms were scanty and no pus cells were seen in the sediment.

Read at the 32nd Annual Meeting of the British Association of Urological Surgeons in London, June 1976.

Table I

Summary of Cases of Inverted Papilloma of Bladder and Posterior Urethra reported in the English Language Literature

Authors	Number	Sex		Age	Main symptoms			Site of Tumour
		Male	Female		Obstruction	Haematuria	Infection	
Potts and Hirst (1963)	1	1		63	+			Bladder neck
Trites (1969)	3	3		56		+		Prostatic urethra
				79	+			Bladder neck
				59			+	Prostatic urethra
Assor and Taylor (1970)	1	1		26		+		Apex of trigone
Sullivan *et al.* (1971)	2	2		71	+			Bladder neck
				45		+		Bladder base
Potts and Hirst (1973)	8	7	1		+	+		* Trigone Posterior urethra
Pienkos *et al.* (1973)	1	1		46		+		Trigone
Cummings (1974)	1	1		68	+			Bladder neck
Matz *et al.* (1974)	1	1		75	+			Bladder neck
Hefter and Young (1975)	1	1		65	+	+		Bladder neck
Henderson *et al.* (1975)	5	5		49-79	+(4)			Bladder neck Left lateral wall
DeMeester *et al.*, (1975)	20	15		44-78	+(10)	+(5)		* Bladder neck (8) Trigone (5) Around ureteric orifices (4) Left lateral wall (1) Posterior urethra (1)
			5	46-62	+(1)	+(1)	+(3)	
Present series	35	33		22-78				
			2	40-61		See Table II		See Fig. 1
Total	79	71	8	22-79				

* Correlation between site and other features not attempted due to lack of information (Potts and Hirst) or complexity (DeMeester *et al.*).

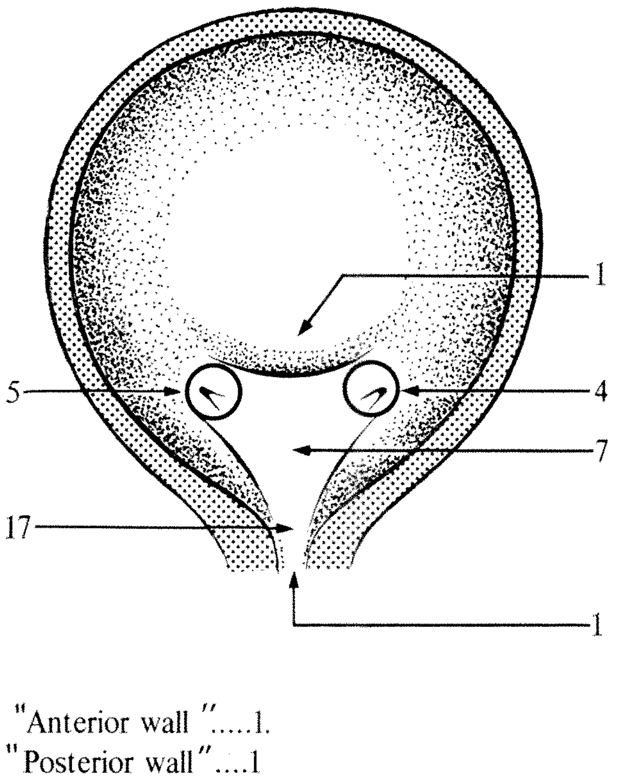


Fig. 1. Inverted papillomas of the lower urinary tract: site of 37 lesions in 35 patients (Groups I and II).

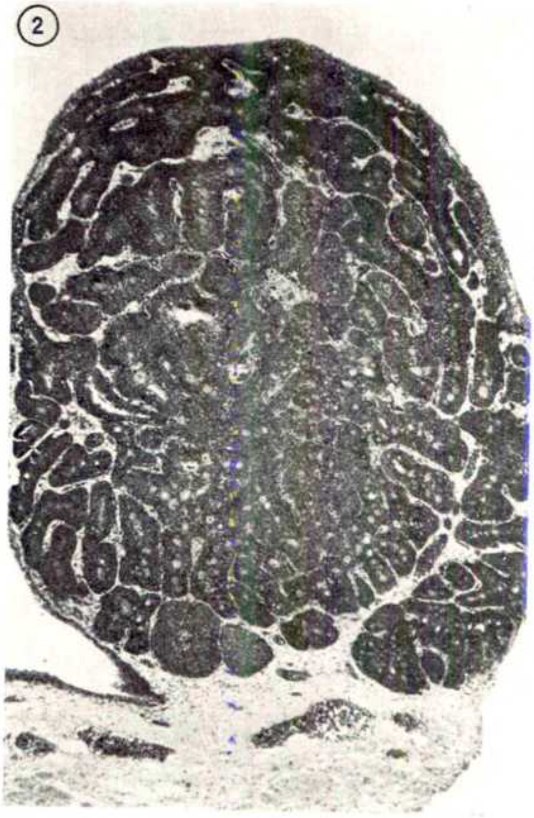
Cystoscopic Appearances

The lesions were sometimes described as "papillomas" but more commonly as solid-looking polyps, often pedunculated, with a smooth or slightly nodular surface; sometimes the adjectives "unusual" or "curious" were applied. The largest estimated size was 3 cm. In 2 men 2 separate lesions were present—making 37 tumours in all (Fig. 1). 17 were situated at the bladder neck, 9 around the ureteric orifices, 7 in the region of the trigone, 1 just above the interureteric bar and 1 in the urethra at the internal meatus. In 2 cases the site was stated to be the anterior and posterior wall respectively without detailed localisation.

Table II

Main Symptoms of the 18 Patients in Group I.

Group I (18 cases)			
Haematuria	7	13	
+ infection	3		
+ obstruction	3		7
Obstruction	4		
Penile soreness	1		
	18		



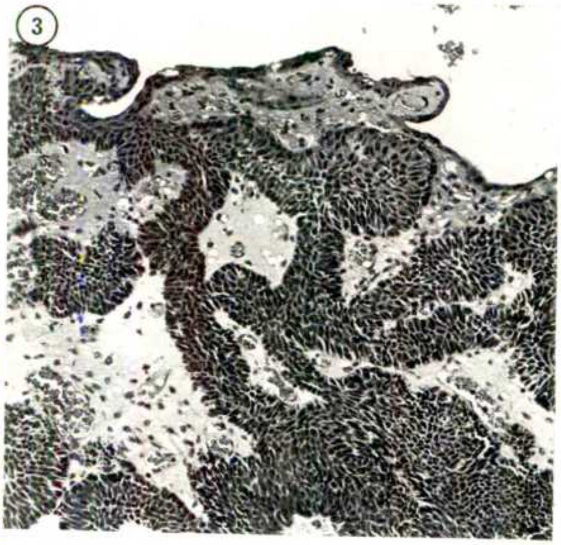


Fig. 2. Small inverted papilloma described as a "curious lesion" on the trigone of a 63-year-old male and showing the typical polypoidal nature of the lesion. H & H × 10. Enlargement × 4.

Fig. 3. Surface of an inverted papilloma showing attenuated covering epithelium, with small surface papillations, from which trabeculae of transitional epithelium extend into the underlying vascular connective tissue. H & H × 40. Enlargement × 4.

Treatment

In each case the lesion was resected, usually endoscopically, and the base fulgurated.

Macroscopic Appearances

As the resected specimens (Group I) consisted frequently of fragments their orientation was often difficult. The fixed tissue was cream to light brown in colour and the cut surface fleshy and homogeneous. The weight of the resected tissue ranged from under 0·1 g to 4·9 g.

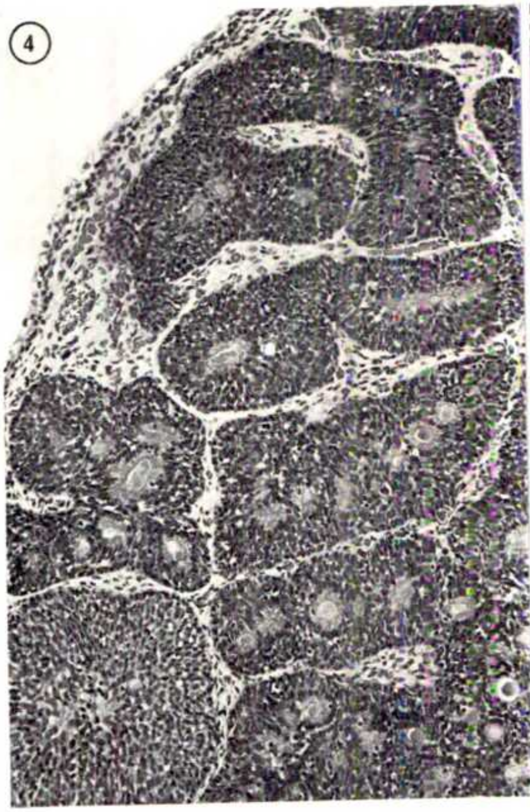
Microscopic Appearances

The typical lesion is polypoidal (Fig. 2) with a surface layer of transitional epithelium, sometimes attenuated. From the surface, trabeculae and nests of similar epithelium extend down into the supporting connective tissue to occupy much of the centre of the polyp. A few tiny surface papillations are sometimes seen (Fig. 3). In some cases the appearances suggest the exuberant formation of von Brunn's nests, which at times show central lumen formation (Fig. 4). The structure of other lesions is more bizarre, with branching and anastomosing cords of epithelial cells roughly twice the thickness of normal urothelium (Fig. 5) and outlined by an intact basement membrane. These epithelial cords resemble papillary processes turned outside in, with the stroma and basal layer of cells on the outside and differentiation occurring towards the centre, where there is sometimes lumen or cyst formation. The outer layers of cells are arranged at right angles to the adjacent basement membrane, while the central ones may be parallel to it, and sometimes show cytoplasmic vacuolation and nuclear pyknosis. Lumina when present (Figs. 4 and 5) are lined by flattened to low columnar cells with basal nuclei, and sometimes contain Alcian Blue-Periodic Acid-Schiff (AB-PAS) positive secretions and occasionally crystals. Focal squamous metaplasia, usually in the form of epithelial whorls, is not uncommon; intercellular bridges are present in these areas, but no keratin. Although a modest degree of cellular pleomorphism is occasionally seen, mitotic figures are characteristically absent or very rare.

The cords of cells are separated by a variable amount of loose delicate stroma, often rich in capillaries. Lymphocytes and plasma cells may be scattered throughout the stroma, but are not usually prominent and, in some cases, are totally absent.

In AB-PAS stained sections, secretion is often coloured by both Alcian Blue and the PAS: cytoplasmic vacuoles of cells lining cystic spaces react similarly. At times inspissated secretions within these spaces show either double staining or more commonly only strong coloration by the PAS. Small amounts of glycogen are present in the cells of areas showing squamous metaplasia. Where the epithelium is looser, especially in foci undergoing cytolysis, pale Alcian Blue staining is seen between the cells. Ground substance of the oedematous stromal tissue is also coloured faintly by Alcian Blue.

Reticulin stains (modified Laidlaw's technique) show fibres in the stroma which surround and clearly outline nests and islands of epithelial cells.



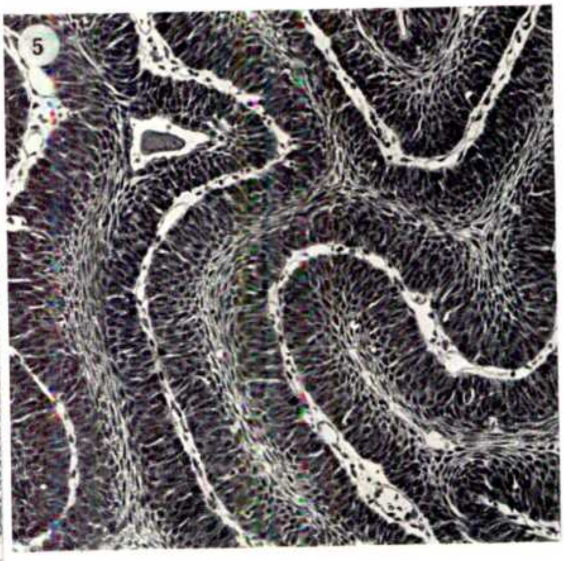


Fig. 4. Same lesion as Figure 2 showing resemblance to von Brunn's nests. H & E ×40. Enlargement ×4.

Fig. 5. Centre of an inverted papilloma showing branching cords of transitional epithelium, roughly twice the thickness of normal urothelium and resembling papillary processes turned outside in. The stroma and basal layers of cells are on the outside and there is central lumen formation in places. H & E ×40. Enlargement ×4.

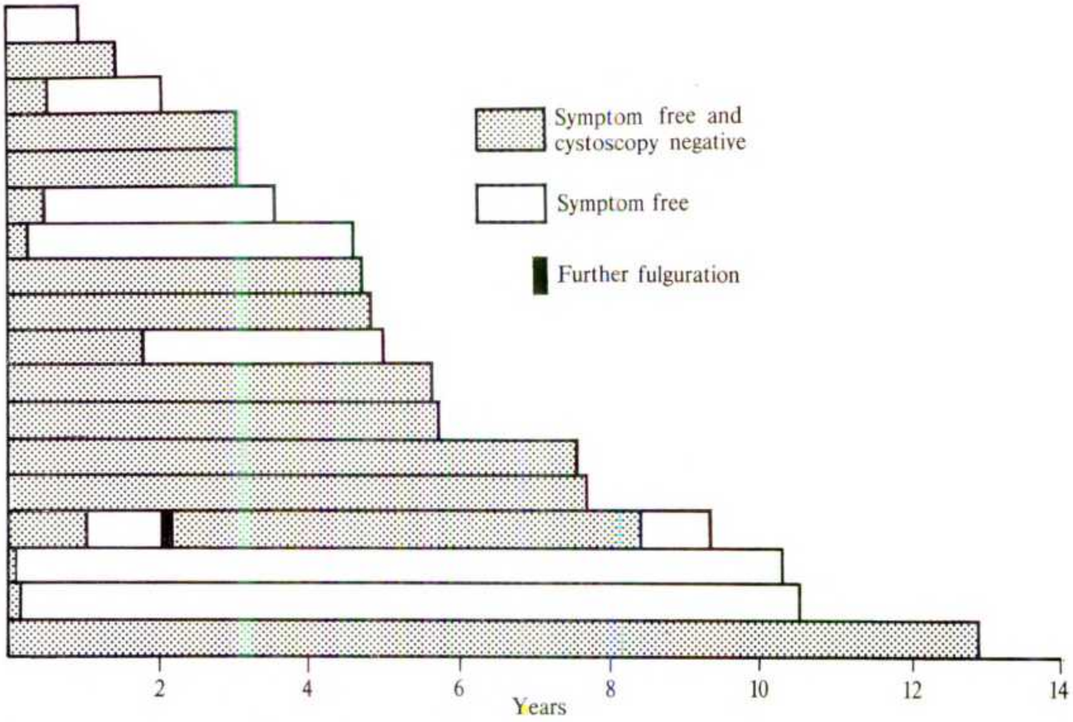


Fig. 6. Follow-up of 18 patients in Group I (St Peter's series).

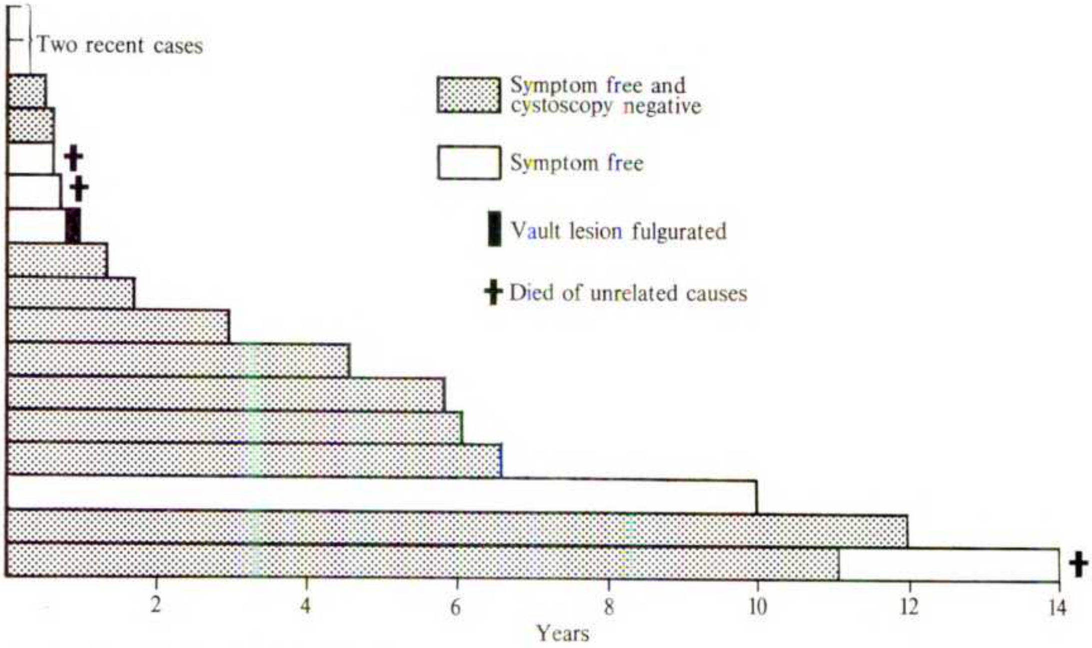
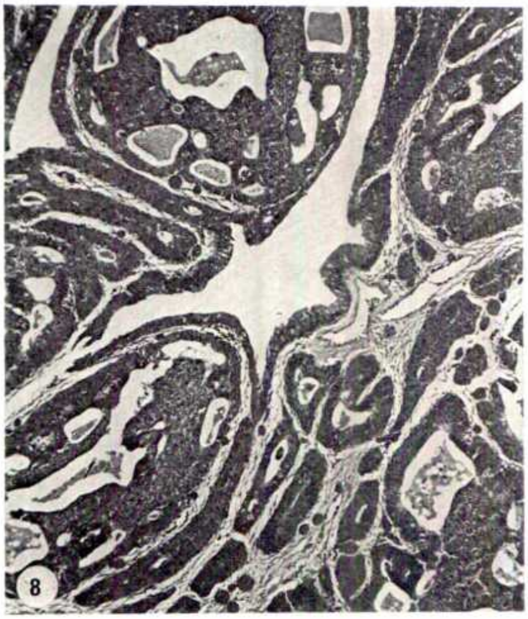


Fig. 7. Follow-up of 17 patients in Group II (referred cases).



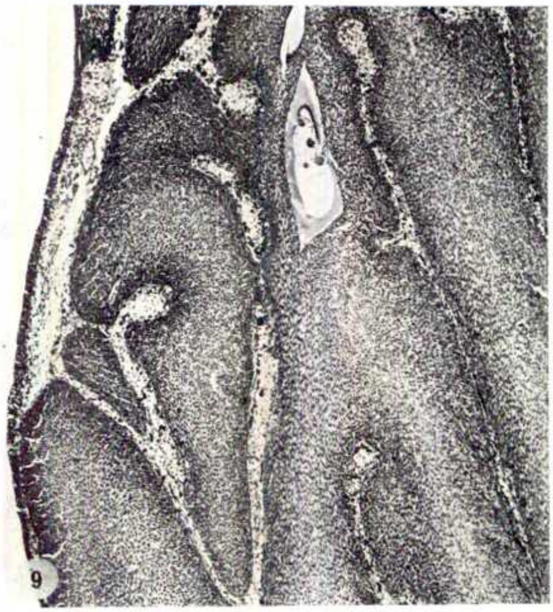


Fig. 8. Tumour from the renal pelvis of a 58-year-old woman showing histological similarity to the inverted papilloma of bladder. H & E × 16. Enlargement × 4.

Fig. 9. Edge of polypoidal transitional cell carcinoma of bladder showing an inverted pattern of growth. Note the surface layer of transitional epithelium and underlying bulbous masses of epithelial cells. H & E × 16. Enlargement × 4.

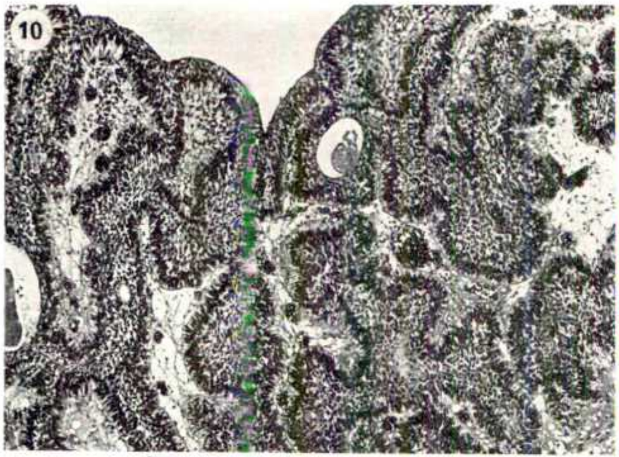
Follow-up

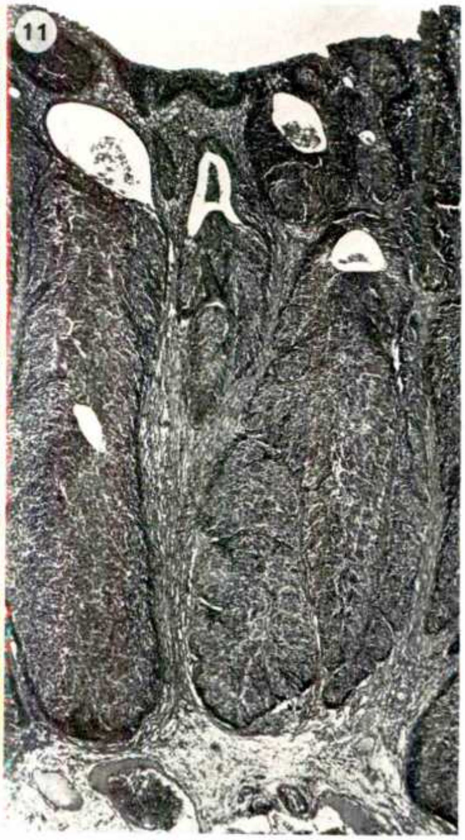
The 18 Group I patients have been followed up for periods ranging from 11 months to almost 13 years (Fig. 6)—11 by regular check cystoscopy. 17 have shown no evidence of local recurrence or any other urothelial lesions. In the 18th man, 2 years after his initial treatment, a tiny "mossy' area was seen on cystoscopy at a short distance from the original site and was fulgurated without a biopsy; his bladder mucosa remains cystoscopically clear 6 years later.

Follow-up information is available also for 15 of the 17 Group II patients (Fig. 7) the remaining 2 cases being too recent to assess. 1 female was found to have a lesion at the bladder vault which was fulgurated without biopsy 9 months after the initial resection. The remainder have developed no further urothelial lesions during periods of up to 14 years, though 3 have died of unrelated causes.

Similar Lesions in the Upper Urinary Tract

A large lesion (maximum dimension 3 cm) with a histological appearance similar to that of the inverted bladder papilloma (Fig. 8), but which arose in the renal pelvis of a 58-year-old female, has been shown to us by Professor A. C. Thackray, formerly of the Middlesex Hospital. The tumour was rather more complex than the bladder lesions in this series but showed essentially the same inverted pattern with very rare mitotic figures and an intact basement membrane. Treatment was by nephroureterectomy. At the same time a Wertheim's hysterectomy was performed for carcinoma of the endometrium, whose spread caused death 4 years later.





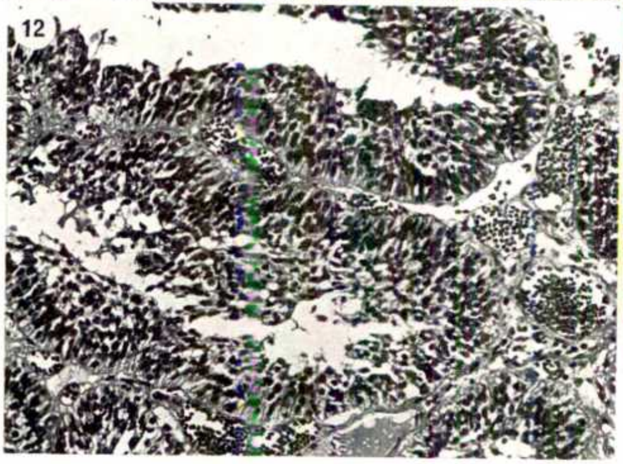


Fig. 10. Area resembling an inverted papilloma in a bladder tumour composed elsewhere of transitional cell carcinoma of both inverted and exophytic pattern (same case as illustrated in Figures 11 and 12). H & E × 16. Enlargement × 4.

Fig. 11. Area of transitional cell carcinoma of inverted pattern in tumour illustrated in Figures 10 and 12. H & E × 10. Enlargement × 4.

Fig. 12. Area of transitional cell carcinoma of exophytic type in a tumour of mixed pattern (same case as illustrated in Figures 10 and 11). H & E × 40. Enlargement × 4.

Other Bladder Lesions having an inverted Papillary Pattern

An inverted pattern is not confined to benign lesions but is seen also in certain carcinomas, the whole or part of which may be of this structure. The tumour illustrated in Figure 9, designated as a transitional cell carcinoma, is of this type and was situated on the posterior wall of the urinary bladder, medial to the left ureteric orifice, in a 66-year-old male; it measures 2·5 × 1·8 × 1·5 cm. The lesion is polypoidal with a surface layer of urothelium from which masses of cells extend downwards into the lamina propria though the basement membrane is everywhere intact. In contrast to the slender trabeculae of the typical inverted papilloma there are bulbous masses of proliferating epithelium showing some differentiation toward the centre in places but rarely cyst formation. Mitotic figures are relatively numerous. The relationship of this lesion to the benign inverted papilloma seems analogous to that of papillary transitional cell carcinoma to transitional cell papilloma. This tumour had been preceded, and was followed, by multiple transitional cell carcinomas which showed both exophytic and inverted features and led to cystectomy 5 years later.

Various patterns of growth may co-exist within a single neoplasm. 1 such tumour, situated at the base of the bladder of a 64-year-old female, contained 1 area indistinguishable from an inverted papilloma (Fig. 10) along with areas of transitional cell carcinoma of both inverted and exophytic patterns (Figs. 11 and 12). This tumour was removed by open diathermy excision followed by radium implant and the patient has remained tumour free for 7 years.

Discussion

33 of the 35 patients with inverted papillomas of the lower urinary tract in this series were men; this concurs with other published cases in which 38 of 44 patients were males. The age range (22 to 78 years) of the patients is also similar to that reported by others, exceptions being two 79-year-olds described by Trites (1969) and Henderson, Allen and Bourne (1975).

Presenting symptoms in this series were not unlike those reported elsewhere (Table I) except that bladder obstruction appeared to be less frequent. In view of the proximity of many of the lesions to the bladder outlet obstructive symptoms are not surprising, though in many cases prostatism may be a contributory factor.

The gross and microscopic appearances resemble closely those described by others. According to Koss (1975) the largest tumour recorded measured 7·5 cm in greatest diameter. The lesion reported by Cummings (1974) is unique in that it is composed entirely of squamous cells.

In addition to Professor Thackray's case, an inverted papilloma of the renal pelvis has been reported by Matz, Wishart and Goodman (1974), and Pienkos, Iglesias and Jablokow (1973) state that Price has also seen such a lesion.

Opinions concerning the histogenesis and nature of the lesion differ. Potts and Hirst (1963) considered it to be a neoplasm and postulated origin from subtrigonal glands but clearly this does not explain the lesions in the renal pelvis.

The epithelium of the trigone and the posterior wall of the urethra down to the ejaculatory ducts—the site of origin of the great majority of the lesions—is generally believed to be of mesodermal origin, differing embryologically from the remainder of the bladder lining which is derived from the endoderm. Is it possible that this mesodermal epithelium, when stimulated, tends to proliferate into the underlying tissue rather than into the bladder cavity? If so then similar lesions would not be unexpected in the renal pelves and ureters which bud from the mesonephric ducts and also originate from mesoderm.

Cummings (1974) believes that persistent or recurrent inflammation secondary to lower urinary tract obstruction causes these lesions. However, this seems unlikely in our patients in whom neither the histological nor the clinical findings support this idea. The significance of the crystalline material seen in a few cases is not clear but is considered secondary rather than primary.

Matz *et al.* (1974) showed by serial sections that their lesions consisted of intercommunicating crypts in continuity with the bladder lumen and considered them to be an exaggerated form of von Brunn's nest formation—that is, hyperplastic rather than neoplastic. Salm (1967) considered his "adenoma" to have originated in von Brunn's nests and cystitis cystica. Origin from "the irritated bladder mucosa of proliferative cystitis" was suggested by DeMeester *et al.* (1975), who saw some mucosal proliferations at the margins in the majority of their lesions. They disagreed with Matz and considered the lesions to be neoplastic. In our specimens the surrounding bladder mucosa was not usually available for study. When a small amount of adjacent epithelium was present, von Brunn's nests were more often absent than present. Nevertheless, parts of some inverted papillomas do resemble the focal proliferative lesions common in bladder (and other) urothelium and such an origin for these tumours is therefore an attractive suggestion.

Whatever its cause we consider this a neoplastic lesion, and if the analogy to the inverting form of transitional cell carcinoma is accepted then one has to consider, as did Trites (1969), that the lesion is an inverting variant of the urothelial papilloma. The benign course in patients with the typical inverted papilloma is well established with only 1 reported recurrence (DeMeester *et al.*, 1975) and no proved subsequent malignancy. The fact that 2 lesions may occur either simultaneously or consecutively does not alter the favourable outlook. Co-existence of inverted papillomatous and carcinomatous areas in some tumours does not necessarily imply that a typical lesion may undergo malignant transformation. It would appear that in the case illustrated in Figure 9 the natural history of the "inverted" form of papillary carcinoma resembles that of the exophytic papillary variety.

The inverted papilloma of the bladder has been likened by some workers to the lesion with the same name seen on the lateral wall of the nose and in the nasal sinuses. There are some important differences. The nasal mucosal lesions consist of essentially epidermoid instead of transitional epithelium; also, crypt formation is much more conspicuous in the nasal lesions with a thicker proliferating epithelium lining sinus tracts which extend downwards from the surface (Michaels and Hyams, 1975). In the nasal passages there is a strong tendency for local recurrence and a few become malignant. In our opinion the nasal lesion resembles the inverted transitional cell bladder carcinoma more than the classical inverted urothelial papilloma.

Summary

A study of 35 cases of inverted papilloma of urothelium confirms that it is a distinctive entity and typically benign.

These lesions occur mainly in males, may be multiple, and are sometimes situated elsewhere than in or near the trigone, which is their characteristic site. Their precise histogenesis remains uncertain.

It must be stressed that not all transitional cell tumours of inverted pattern are of this type; some will have the appearance of and behave as malignant tumours.

The same diagnostic criteria of malignancy established for the more common exophytic papillary neoplasms must be applied also to the inverted papillary tumours herein described.

We thank Dr R. C. B. Pugh and Professor R. W. Mowry for their very helpful advice in the preparation of this paper and also the Departments of Medical Art and Medical Photography of the Institute of Urology.

We are also grateful to those who referred the cases in Group II for permission to use their material and for their help with the follow-up.

References

Assor, D. and Taylor, J. N. (1970). Inverted papilloma of the bladder. *Journal of Urology*, **104**, 715-717.

Cummings, R. (1974). Inverted papilloma of the bladder. *Journal of Pathology*, **112**, 225-227.

DeMeester, L. J., Farrow, G. M. and Utz, D. C. (1975). Inverted papilloma of the urinary bladder. *Cancer*, **36**, 505-513.

Hefter, L. G. and Young, I. S. (1975). Inverted papilloma of bladder. *Urology*, **5**, 688-690.

Henderson, D. W., Allen, P. W. and Bourne, A. J. (1975). Inverted urinary papilloma. Report of five cases and review of the literature. *Virchows Archiv A, Pathological Anatomy and Histology*, **366**, 177-186.

Koss, L. G. (1975). Tumors of the urinary bladder. *Atlas of Tumor Pathology*, 2nd series, fascicle 11. Washington, D.C., Armed Forces Institute of Pathology, pp. 10-12.

Matz, L. R., Wishart, V. A. and Goodman, M. A. (1974). Inverted urothelial papilloma. *Pathology*, **6**, 37-44.

Michaels, L. and Hyams, V. J. (1975). Objectivity in the classification of tumours of the nasal epithelium. *Postgraduate Medical Journal*, **51**, 695-707.

Paschkis, R. (1927). Über Adenome der Harnblase. *Zeitschrift für Urologische Chirurgie*, **21**, 315-325.

Pienkos, E. J., Iglesias, F. and Jablokow, V. R. (1973). Inverted papilloma of bladder. *Urology*, **2**, 178-179.

Potts, I. F. and Hirst, E. (1963). Inverted papilloma of the bladder. *Journal of Urology*, **90**, 175-179.

Potts, I. F., and Hirst, E. (1973). Inverted papilloma of the bladder. 16th Congress of the International Society of Urology, Amsterdam. Part 2, Paris: Doin, 535.

SALM, R. (1967). Neoplasia of the bladder and cystitis cystica. *British Journal of Urology*, **39**, 67-72.
SULLIVAN, J. J., WATSON, J. G., KINGSTON, C. W. and YAXLEY, R. P. (1971). Inverted papilloma of the urinary bladder: a report of two cases. *Australian and New Zealand Journal of Surgery*, **41**, 60-62.
TRITES, A. E. W. (1969). Inverted urothelial papilloma: report of two cases. *Journal of Urology*, **101**, 216-219.

The Authors

Katharine M. Cameron, FRCPath, Senior Lecturer in Pathology, Institute of Urology.
Charles H. Lupton, Jr., MD, Visiting Professor, Department of Pathology, St Peter's Hospitals (Professor of Pathology, University of Alabama in Birmingham, USA).

Request for reprints to Dr K. Cameron, Department of Pathology, St Paul's Hospital, 24 Endell Street, London WC2.

British Journal of Urology (1976), **48**, 579-586 ©

The Value of Lymphography in the Management of Bladder Cancer

A. G. TURNER, W. F. HENDRY, J. S. MACDONALD and D. M. WALLACE
Departments of Urology and Radiology, Royal Marsden Hospital, London

The value of lymphography in the assessment of bladder cancer has been controversial. In 1969, Lang suggested that lymphography may have "little or no value in the assessment of early metastatic involvement of the regional nodes of the bladder, especially the obturator and internal iliac nodes". On the other hand, several recent reports with careful radiological and pathological correlation have shown that lymphography may be accurate in up to 94% of cases (Wajsman *et al.*, 1975; Johnson *et al.*, 1976). These reports, however, concerned relatively small numbers of patients, and no long-term survival data were presented in relation to the findings on lymphography.

In this study, we report on 11 years' experience with lymphography at the Royal Marsden Hospital. Particular emphasis has been placed on its relation to patient survival, and its accuracy as confirmed by operative histological findings.

Methods

237 patients with histologically proven carcinoma of bladder were studied by pedal lymphography, between 1964 and 1975, using the technique described by Macdonald and Wallace (1965). The details of radiological interpretation have been previously described by Higgs and Macdonald (1968).

Table I

Overall Results of Lymphography—228 cases

	Initial diagnosis	Review after 2 months	Final diagnosis
Positive	90	60/65 Positive 5/65 Negative	91
Suspicious	29	4/23 Positive 19/23 Negative	(6)
Negative	109	2/87 Positive 89/87 Negative	131

All cases were assessed by cystoscopy, biopsy and bimanual examination under general anaesthesia at this hospital. The tumours were classified by the TNM system as recommended by the UICC (Wallace, Chisholm and Hendry, 1975). Tumour histology from other hospitals was also reviewed.

Read at the 32nd Annual Meeting of the British Association of Urological Surgeons in London, June 1976.

In all instances, the radiologist's report made at the time was used in this analysis, and no reports have been reviewed retrospectively for the purposes of this study. However, particular emphasis has always been placed on the value of follow-up films so that node behaviour could be assessed during and after treatment. In some cases, the initial radiological diagnosis was modified as a result of these follow-up studies (Table I). In this study the final diagnosis has been used in the overall assessment of results.

In 70 cases, lymph nodes systematically removed at operation were studied histologically, and the pathological and radiological findings were compared, taking into account any radiotherapy which may have been given between the lymphogram and operation.

Follow-up for the purposes of this study has been taken from the date of the lymphogram.

Results

228 patients underwent bilateral lymphography and in 9 cases only unilateral injection was possible. The overall results in 228 cases of bilateral lymphography are shown in Table I. As a result of the follow-up films taken after an interval of 2 months or more, the diagnosis was altered from positive to negative in 5 cases, and from negative to positive in 2 cases. These follow-up films allowed an initial diagnosis of "suspicious" in 29 cases to be resolved into positive in 4 cases, or negative in 19 cases. In 6 "suspicious" cases no follow-up was available, and these cases are excluded from further study. Thus, the final analysis comprises 91 positive and 131 negative lymphograms.

The distribution of disease in the 91 positive lymphograms and its relation to the site of the primary bladder tumours is shown in Tables II and III. Para-aortic node involvement was at

Table II

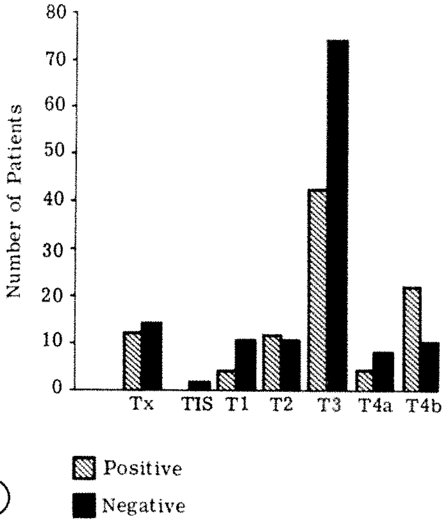
Distribution of Disease (91 Positive Lymphograms)

Positive iliac nodes		Positive para-aortic nodes
Unilateral	39	9 (23%)
Bilateral	52	28 (54%)

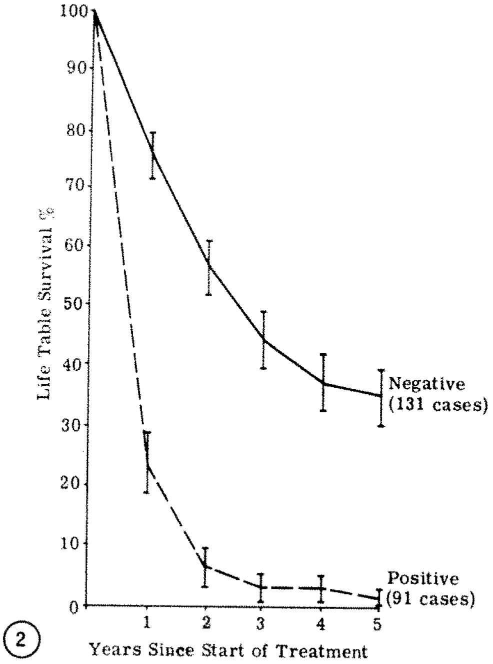
Table III

Distribution of Disease on Lymphography Related to Site of Bladder Tumour (91 Positive Cases)

Site of bladder tumour	Number of cases	Iliac nodes positive R	L	Bilat.	Para-aortic nodes positive
Right	26	10	2	– 14	1 8
Left	27	0	10	– 17	4 8
Base	13	4		– 9	0 8
Dome and posterior wall	16	7		– 9	4 7
Unknown	9	–		–	–



①



②

Fig. 1. Results of lymphography related to classification of primary bladder tumour.

Fig. 2. Survival by lymphogram results.

least twice as common when the iliac nodes were involved bilaterally. Iliac nodes were generally involved on the ipsilateral side, but in 2 cases isolated contralateral spread was observed.

The results of lymphography are related to the T-classification of the primary bladder tumour in Figure 1. Many of these cases were referred to this hospital after previous treatment elsewhere; the incidence of positive lymphograms does *not* therefore represent the true incidence of lymph node metastases at presentation. It is of interest to note that positive lymphograms were occasionally found in T1 tumours, and that metastases appeared to be more common with fixed (T4b) tumours compared to those involving adjacent organs (T4a).

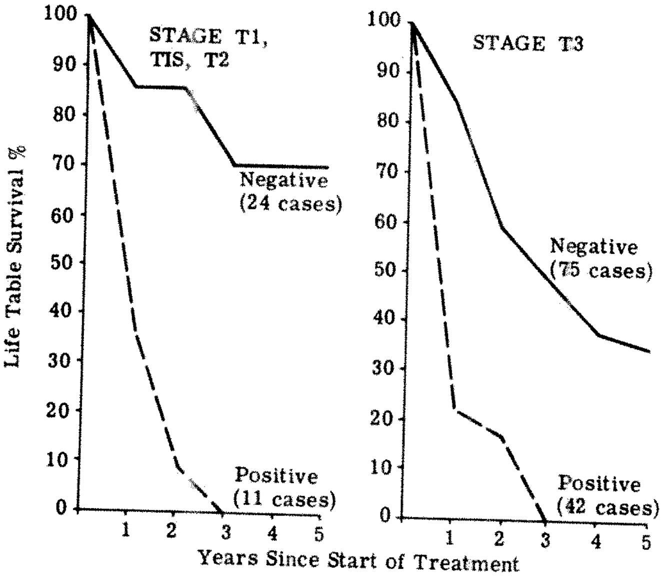
The results of the lymphograms were also analysed in relation to duration of symptoms and known duration of tumour, tumour size and histological grade, but, surprisingly, no clear-cut correlations could be found.

Survival

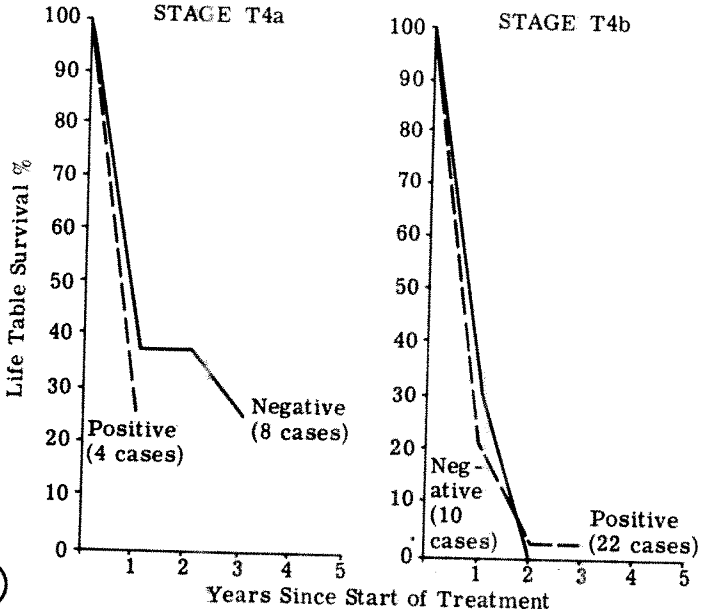
The overall Life-Table survival rate of patients with positive and negative lymphograms is shown in Figure 2, and survival rates related to T-classification of the primary bladder tumours are shown in Figures 3 and 4. The extremely poor prognosis associated with positive lymphography is clearly shown. However, it may be seen from Figure 5 that a few cases (6·4%) with unilaterally positive iliac nodes survived to 5 years, whereas no patient with bilateral iliac or para-aortic nodes positive lived for more than 3 years.

Histological Correlation

The histological findings in lymph nodes removed at operation in 70 cases are related to lymphographic assessment in Table IV, and further analysed in relation to preoperative radiotherapy



③



④

Figs. 3 and 4. Survival by bladder tumour stage and lymphogram result.

in Tables V and VI. Of 42 cases with negative lymphograms, 6 showed microscopic evidence of node involvement (false negative rate 14·3%). On the other hand, of 28 lymphographically positive cases, no tumour was found in the nodes in 6 patients. 5 of these patients had had intervening radiotherapy (4,000 rads to the whole pelvis) which may have "sterilised" the nodes. In the 6th case, co-existing tumour was present in the upper urinary tract, and the node biopsy taken may not have been representative.

Excluding the 5 patients who received preoperative radiotherapy, the overall concordance between lymphography and subsequent operative node histology was 58/65 cases (90%).

Development of Metastases

The incidence of clinical development of distant metastases and the evidence of metastases at autopsy are related to the lymphogram results in Table VII. Only 9% of patients with negative lymphograms developed metastases, although 4% of these were present at the time the lymphogram was performed. There was a much higher incidence of distant metastases (33%) in patients with positive lymphograms, and of these 10% were present when the lymphogram was done. The difference in the incidence of metastases was confirmed at autopsy.

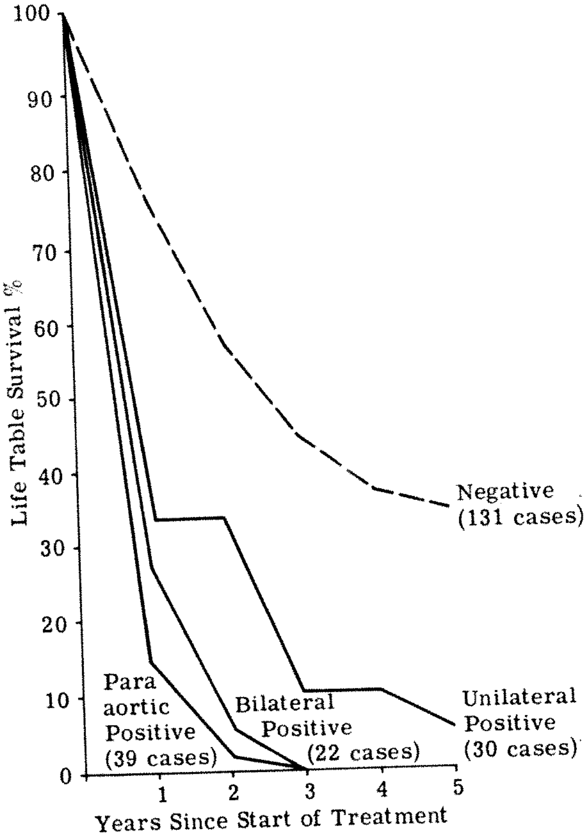


Fig. 5. Survival by site of positive lymphogram findings.

Table IV

Histological Findings in Lymph Nodes Removed at Operation Related to Lymphographic Assessment (70 Cases)

	Histology	
Lymphogram	Negative	Positive
Negative (42 cases)	36	6
Positive (28 cases)	6	22

Table V

Histological Findings in Lymph Nodes Removed at Operation in 42 Patients with Negative Lymphograms

		Histological findings			
			Positive		
			Iliac		
Pre-operative radiation	Number of cases	Negative	Right	Left	Para-aortic
None	2	2	–	–	–
4,000 rads	30	26	2	2	0
6,000 rads	10	8	1	0	1

Table VI

Histological Findings in Lymph Nodes Removed at Operation in 28 Cases with Positive Lymphograms, Related to Preoperative Radiotherapy

		Histological findings			
			Positive		
			Iliac		
Pre-operative radiation	Site of radiologically involved nodes (number of cases)	Negative	Right	Left	Para-aortic
None (15 cases)	Iliac: right (3)	0	3	1	1
	bilateral (2)	0	1	1	1
	Para-aortic: (10)	1	6	6	5
4,000 rads (11 cases)	Iliac: right (3)	3	0	0	0
	left (3)	1	2	2	0
	bilateral (2)	1	1	0	0
	Para-aortic: (3)	0	2	1	3
6,000 rads (2 cases)	Iliac: right (1)	0	1	0	1
	bilateral (1)	0	0	1	0

Table VII

Clinical and Autopsy Evidence of Distant Metastases Related to Findings on Lymphography

Lymphography	Number	Distant metastases	
		Clin.	Autopsy
Negative	131	12 (9%)	28 (21%)
Positive	91	30 (33%)	51 (56%)

Discussion

The accuracy and value of any staging procedure in relationship to patient management must be established before it can be recommended as a routine. The technique of lymphography is a consistently successful investigation, as shown by the fact that bilateral demonstration of the nodes was possible in 228/237 cases. With satisfactory patient selection it is a safe technique, and no major lung complications were recorded in this series.

The interpretation of the radiological findings have been discussed in detail previously (Higgs and Macdonald, 1968). It is generally accepted that the obturator and internal iliac nodes may not be filled by this technique. However, since microscopic deposits in these nodes can never be excluded with infiltrating bladder cancer, they should probably always be included within the fields of primary radiotherapeutic or radical surgical treatment. What is vitally important in planning treatment is knowledge of the presence or absence of gross involvement of nodes beyond those in the immediate vicinity of the bladder. It is clear that lymphographically demonstrable deposits in these nodes have a profound influence on the prognosis, and this should affect the treatment policy. In some cases radical ablative surgery may be avoided. Future studies may show a need for adjunctive chemotherapy in other cases, in view of the demonstrably higher incidence of distant metastases.

If lymphography is to be used routinely in the selection of treatment for patients with infiltrating bladder cancer—and to date we have not allowed anything other than the grossest of node involvement to affect patient management—it is essential to establish whether the radiological findings can be confirmed by node histology defined at operation. This study showed a correlation of 90%, and this accords well with figures of 87·5% (Camey, Leduc and Khoury, 1973), 90% (Johnson *et al.*, 1976) and 94% (Wajsman *et al.*, 1975) reported from other centres.

The survival data show that a positive lymphogram is associated with a poor prognosis, especially if node involvement is bilateral or extends to the para-aortic region. Since the Royal Marsden Hospital is a specialist hospital, and many cases were referred after failure of primary treatment elsewhere, the incidence of positive lymphograms in this series does *not* represent the true incidence of node involvement at presentation. Analysis of many features of the primary bladder tumour could not be positively correlated with the findings on lymphography. We therefore believe that this investigation is fundamental in the assessment of patients with *infiltrating* bladder cancer, the TNM categorisation, and the selection of the most appropriate treatment.

Summary

228 bilateral pedal lymphograms in patients with bladder cancer have been correlated with the features of the primary bladder tumour and patient survival. In 70 cases, radiographic findings were correlated with operative node histology.

The results show that it is not possible to predict accurately which cases have lymphatic spread without this investigation. Positive lymphograms were found in 91 cases, and were associated with a very poor prognosis. Only 6% of patients with unilaterally involved iliac nodes survived 5 years, and all patients with bilateral iliac or para-aortic disease died within 3 years.

Histological correlation was found in 90% of cases, and the results indicate that this investigation slightly underestimates the incidence and extent of microscopic lymphatic metastases.

It is concluded that this investigation is essential in planning the treatment of infiltrating bladder tumours.

References

Camey, M., Leduc, A. and Khoury, S. (1973). Intérêt de la lymphographie dans l'exploration du cancer de la vessie. *Journal d'Urologie et de Néphrologie*, **79**, (12, pt 2) 370-372.

Higgs, B. and Macdonald, J. S. (1968). Lymphography in the management of urinary tract tumours. *British Journal of Urology*, **40**, 727-735.

Johnson, D. E., Kaesler, K. E., Kaminsky, S., Jing, B. S. and Wallase, S. (1976). Lymphangiography as an aid in staging bladder carcinoma. *Southern Medical Journal*, **69**, 28-30.

Lang, E. K. (1969). The roentgenographic assessment of bladder tumours. A comparison of the diagnostic accuracy of roentgenographic techniques. *Cancer*, **23**, 717-724.

Macdonald, J. S. and Wallace, E. N. K. (1965). Lymphangiography in tumours of the kidney, bladder and testicle. *British Journal of Radiology*, **38**, 93-99.

Wajsman, Z., Baumgartner, G., Murphy, G. P. and Merrin, C. (1975). Evaluation of lymphangiography for clinical staging of bladder tumours. *Journal of Urology*, **114**, 712-714.

Wallace, D. M., Chisholm, G. D. and Hendry, W. F. (1975). TNM classification for urological tumours (UICC) 1974. *British Journal of Urology*, **47**, 1-12.

The Authors

A. G. Turner, B.Sc, FRCS, Lecturer in Urology.
W. F. Hendry, ChM, FRCS, Consultant Urologist.
J. S. Macdonald, DMRD, FFR, Consultant Radiologist
D. M. Wallace, OBE, MS, FRCS, Emeritus Consultant Urologist (now Professor of Urology, University of Riyadh, Saudi Arabia).

British Journal of Urology (1976), **48**, 587-594 ©

The Management of Deeply Infiltrating (T_3) Bladder Carcinoma: Controlled Trial of Radical Radiotherapy versus Preoperative Radiotherapy and Radical Cystectomy (First Report)

D. M. WALLACE and H. J. G. BLOOM

Royal Marsden Hospital and Institute of Cancer Research and Institute of Urology, London

For the Clinical Trials Group[1], Institute of Urology

Cure rates following radical cystectomy for patients with infiltrating bladder cancer involving the deep muscle or perivesical tissue (stage T_3 or B_2C) have been, and continue to be, very disappointing: not more than about 20% of such cases survive 3 years following this operation. At least comparable results have been achieved by radical supervoltage irradiation without the morbidity and mortality and the loss of urinary and sexual function associated with radical surgery. In recent years there has been an improvement in the reported results for radiotherapy and now it seems that we may expect, at best, approximately 30% of T_3 cases to survive 3 years, and about 20%, 5 years following radical megavoltage treatment.

The high incidence of residual or recurrent disease in the bladder following radical radiotherapy for deeply invasive tumours, and the failure to obtain better survival rates by radical surgery, have led to the introduction of planned preoperative irradiation with the aim of rendering the tumour more susceptible and more suitable for extirpation by cystectomy, a combined procedure largely pioneered by Dr Whitmore and his colleagues at the Memorial Hospital, New York.

The aim of preoperative irradiation in the treatment of cancer is to reduce tumour size and viability without adding significantly to the postoperative morbidity and mortality. Actively growing, well-oxygenated peripheral tumour extensions, and perhaps limited metastases in regional nodes, may be particularly vulnerable. It is thereby hoped that the margin of resection will be increased, and that the risk of spill and of dissemination of malignant cells at the time of surgery will be reduced, especially during lymph node dissections. Finally, the operation will remove any residual, radio-resistant primary tumour core.

Over the past 5 years a number of workers have initiated combined irradiation and surgery treatment programmes for bladder cancer, principally in the United States and in Holland, but most of these are not randomised studies.

Controlled Therapeutic Trial for Deeply Infiltrating Bladder Cancer (Stage T_3)

In 1966 the Urological Unit at the Royal Marsden Hospital embarked on a strictly controlled study to ascertain whether preoperative irradiation followed by radical cystectomy is a better treatment than radical radiotherapy alone for tumours involving deep muscle or the perivesical

---

[1] J. P. Blandy, V. M. Dalley, J. D. Fergusson, J. E. Freeman, H. G. Hanley, W. F. Hendry, H. F. Hope-Stone, N. Howard, D. Innes Williams, C. H. Kinder, J. Magri, J. M. McArthur, D. O'Connell, D. A. Packham, P. F. Philip, R. C. B. Pugh, W. Shanks, R. T. Turner Warwick, P. F. Wale, R. J. M. Whittle, J. E. A. Wickham, G. B. Williams, J. P. Williams.

Read at the 32nd Annual Meeting of the British Association of Urological Surgeons in London, June 1976.

Table I

T_3 Bladder Cancer Trial: Criteria for Selection

Age not over 70
Histological confirmation
Depth of infiltration clinically into deep muscle or perivesical
No evidence of metastases
No previous major surgery or radiotherapy
Patient fit for radical radiation or radical surgery
Satisfactory renal function
Follow-up at 3-monthly intervals possible

tissue (Bloom, 1971). 2 years later, in 1968, 7 other centres joined in the study which then proceeded under the sponsorship of the Institute of Urology.

Patients for inclusion in the trial were selected on the criteria shown in Table I. Cases were centrally randomised to 1 of 2 treatment groups as follows:

1. Preoperative cobalt or supervoltage X-ray therapy to a dose of 4,000 rads in 4 weeks given as 5 daily fractions per week to the pelvic cavity, including the lymph nodes up to the level of the lower border of the 5th lumbar vertebra. After a rest interval (at home) of 4 weeks, radical cystectomy was performed which included complete excision of the bladder, perivesical tissue, prostate and pelvic nodes. In males, the anterior urethra was not removed unless involved by tumour. In females, routine urethrectomy was recommended.
2. Radical radiotherapy consisting of 6,000 rads to the bladder and 4,500-5,000 rads to the pelvic walls in 6 weeks using 5 daily fractions per week. A 2-phase technique was recommended, the first being that already described for preoperative irradiation, to deliver 4,000 rads to the greater part of the pelvis in 4 weeks. The second consisted of irradiating a smaller volume containing the bladder and perivesical tissue to an additional dose of 2,000 rads in 2 weeks.

The total number of patients entering the trial between 1966 and 1975 from all 8 co-operating centres was 199. 10 cases have been excluded for trial violations relating to patient's age, error in diagnosis or lack of information, leaving 189 for study (Table II). The number of cases by co-operating centre is shown in Table III: the distribution is fairly uniform apart from the Royal Marsden which, with a start of 2 years, has contributed 44% of the total material. 91 cases were randomised to receive radical radiotherapy and 98, the combined treatment. Of these, 170 (90%) are now eligible for a 3-year follow-up, and 111 (60%) for 5 years.

Table II

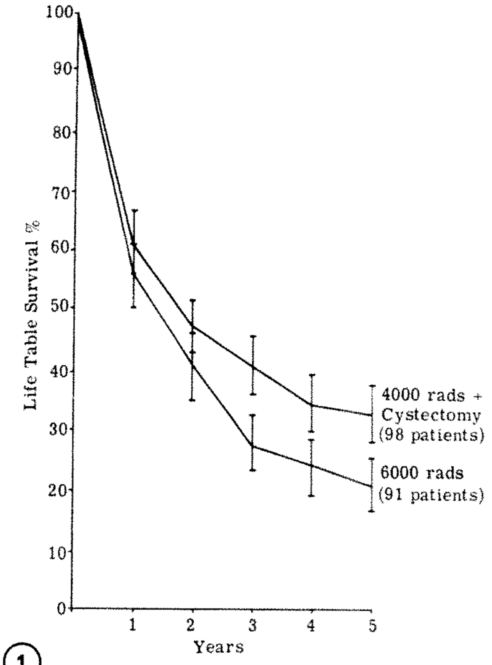
T_3 Bladder Cancer Trial, Inst. of Urology and Co-op. Hospitals (1966-75)

Royal Marsden		1966-75
Inst. Urology and Co-op. Hospitals		1968-75
Total cases entered		199
Exclusions		
Age > 70	5	
Diagnostic error	3	10
Inadequate information	2	
Eligible cases		189

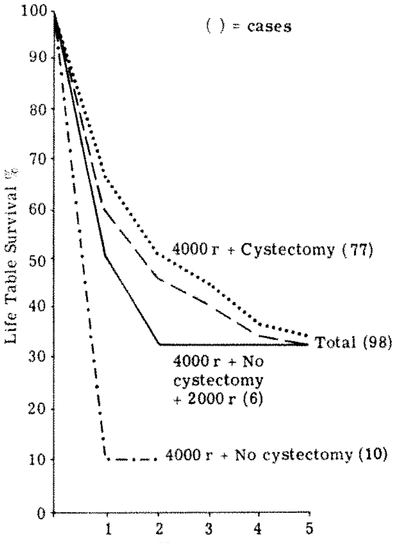
Table III

Cases by Co-operating Hospital

St Bartholomew's	13
Charing Cross	19
Guy's	13
Inst. Urology Group	17
King's College	12
London	19
Oldchurch	13
Royal Marsden	83
Total	189



①



②

Fig. 1. Survival by protocol treatments.

Fig. 2. Preoperative radiotherapy and cystectomy group: survival by actual treatment received.

Results

Figure 1 shows the overall results according to planned protocol treatment. After the first year, during which there is a rapid and profound mortality, the survival curves diverge: the 3- and 5-year survival rates following preoperative irradiation combined with surgery are 41% and 33% respectively, compared with only 28% and 21% for radical radiotherapy. Points plotted on each side of the survival curves represent 1 standard error (calculated by the method of Greenwood).

The probability that the differences in survival rates observed at 3 years is due to chance is approximately *1 in 15* ($P = 0{\cdot}064$), and at 5 years, *1 in 13* ($P = 0{\cdot}077$). In other words, the difference between the 2 treatments has not yet reached the generally accepted significance level of *1 in 20* ($P < 0{\cdot}05$) but the trend for superior results following the combined treatment is undoubtedly present, at least up to 5 years. Further follow-up is required to reveal whether the difference is maintained or not with the passage of time.

For various reasons, 6 patients allocated to radical radiotherapy, and 21 to radiotherapy and surgery failed, to proceed to, or complete, the protocol treatment as planned (Table IV). The combined treatment, involving major surgery, is necessarily more selective in randomised cases than radiotherapy alone. Thus, within the group of 98 patients allocated to the combined treatment, 77 actually received the protocol procedure and 21 did not. The survival curves for the entire group and also according to treatment actually received are shown in Figure 2. Note the early high mortality among the small group of 10 cases receiving incomplete treatment of only 4,000 rads. In contrast, note the relatively good prognosis of the 6 selected cases who, although not proceeding to the planned operation, completed high dose irradiation.

The survival of the 85 cases treated by protocol radical radiotherapy is shown in Figure 3: 30% survived 3 years and 23%, 5 years. In 18 patients a salvage cystectomy was carried out for

Table IV

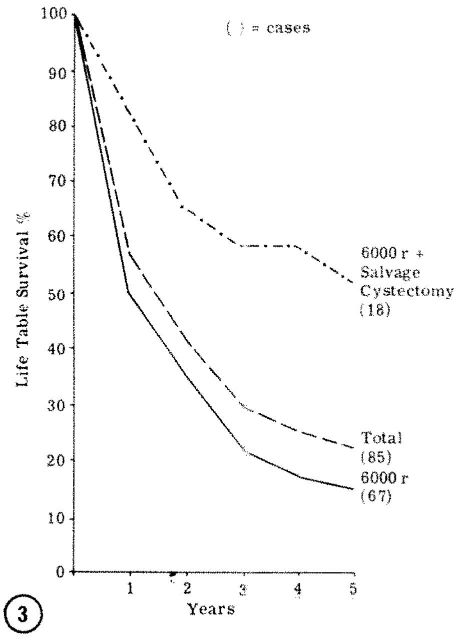
Failing to Complete Planned Treatment

Reason	Radical Rt.	Preop. Rt. + Surg.
Medically unfit	2	5
Inoperable	–	5
Onset of mets.	3	5
Delay in op./policy change	1	4
Refused op.	–	2
Total	6	21

Completing protocol treatment: Radical radiotherapy 85/91; Preop. Rt. + Surgery 77/98.

residual or recurrent tumour, in all but 1, within 18 months of completing radiotherapy. The survival of this small group of cases is remarkably high, the 3- and 5-year rates being 59% and 52%, respectively. The removal of these cases from the total group reduces the survival rate of patients receiving radical radiotherapy by 8%. It is important to stress that these 18 cases are highly selected for radical surgery and their good survival may be due, at least in part, to the high dose pre-surgical irradiation.

Delayed radical cystectomy after failed radical radiotherapy for T_3 tumours can save lives, but in the past often at the cost of an increased operative mortality of 15 to 20%. This loss can



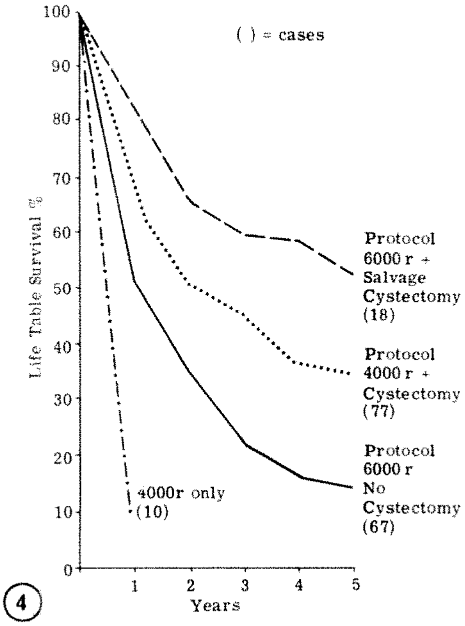


Fig. 3. Radical radiotherapy group: survival by actual treatment received.

Fig. 4. Survival by actual treatment received.

Table V

T_3 Bladder Cancer Trial: 4,000 rads + Cystectomy,
Down-staging and Node Involvement

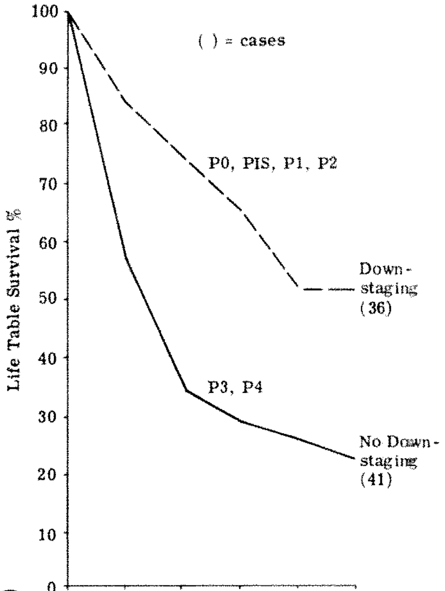
Path. stage	Cases	L. nodes + ve
P0, PIS, P1, P2	36 (47%)	3 (8%)
P3, P4	41 (53%)	15 (37%)
Total	77	18 (23%)

probably be reduced and the overall survival rate increased by recognising radiotherapy failures at an early date and by introducing surgery before advanced fibrosis has become established. In this trial the operative mortality (within 2 months) for the 18 cases of salvage cystectomy was 11% (2 of 18 cases).

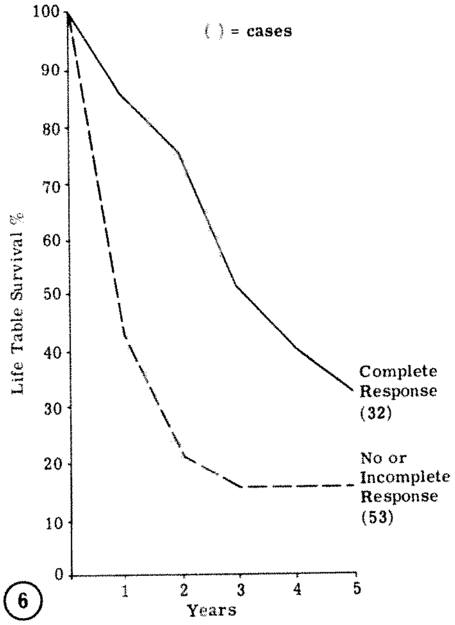
The results of the trial to date are summarised in Figure 4.

Results by Radiation Response

The surgical specimen from the 77 patients treated by preoperative irradiation and radical operation was examined for the extent of residual primary tumour and the state of the regional lymph nodes in order to try and assess the response to the limited irradiation (Table V). In 36 of the 77 cases (47%) there was reduction in the pathological stage (P), compared with the original



⑤



⑥

Fig. 5. 4,000 rads and cystectomy: survival by radiotherapy response: pathological downstaging. (Excluding 21 cases not completing planned treatment.)

Fig. 6. 6,000 rads. Survival by *clinical* response to radiotherapy.

clinical state (T) of which 64% showed no residual cancer or only *in situ* changes. Similar results have been reported in other series where doses of 4,000-5,000 rads have been administered.

The overall incidence of nodal metastases was 23% and in the presence of a good response of the primary tumour to irradiation, only 8% (Table V). The expected proportion of node-positive cases with *un*irradiated T_3 tumours is 40 to 50%. This observation suggests that preoperative irradiation may be a particularly effective treatment for some patients with limited metastases in regional nodes. In other words, a good radiation response observed in the primary tumour, leading to stage reduction, is associated with a good response of nodal metastases.

The fate of patients according to irradiation response following 4,000 rads preoperatively is shown in Figure 5. Of 36 cases in which down-staging was present in the subsequent surgical specimen, the 3- and 5-year survival rates were 66% and 51%, respectively. The corresponding survival rates for 41 patients showing no such change was only 29% and 22%. Thus, the survival rate for patients showing a good response to irradiation was more than twice as great as that for non-responders. Good cases for radiotherapy also seem to be good cases for subsequent surgery.

A striking difference in survival is also seen in "responders" and "non-responders", based on *clinical* assessment, following radical radiotherapy (Fig. 6). Thus, the 2-year survival rate for patients showing a *complete* response is 75%, compared with only 22% for non or partial responders.

Combined Treatment: Operative Mortality and Survival by Age

The overall operative mortality within 2 months following protocol radical surgery after preoperative irradiation was 7·8% (6/77). This was related to age, being 5·5% for patients under 60, 8·7% for those aged 60 to 64, and 11% for those aged 65 to 70.

For the age-groups under 60, and between 60 and 64, the combined treatment gave results superior to those of radical radiotherapy, but in the group aged 65 and over, the results for the 2 treatments were virtually the same (Figs. 7-9). Thus, for older patients radical radiotherapy appears to be the treatment of choice.

Future Studies

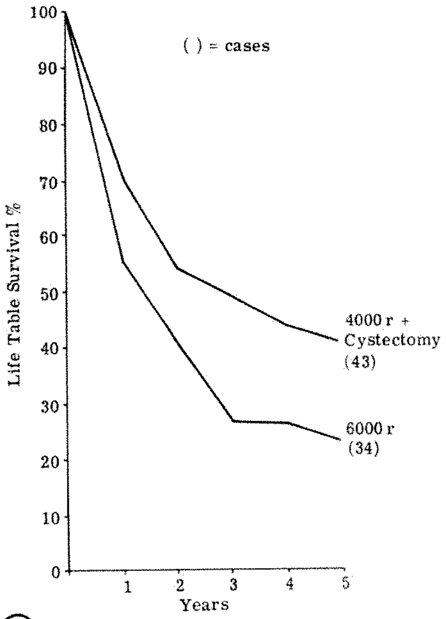
Only 40 to 50% of T_3 bladder cancers show a substantial response to preoperative irradiation using 4,000 rads. Our aim in such cases should be to achieve a greater incidence and degree of tumour regression, since this may be a major factor in attempting to increase the success of subsequent radical surgery in the multimodal treatment of the disease.

Raising the dose of irradiation alone is unlikely to achieve a much greater response, since in this study *complete* clinical tumour regression was seen in only 38% of the cases treated with 6,000 rads, and such doses may carry an increased morbidity and mortality risk for radical surgery. A greater tumour regression rate could perhaps be achieved by the use of chemical radiosensitising agents such as the nitroimidiazole and nitrofuran derivatives, or by adjuvant cytotoxic chemicals such as methotrexate (Hall *et al.*, 1974) which may have the additional merit of destroying distant micrometastases outside the irradiated volume.

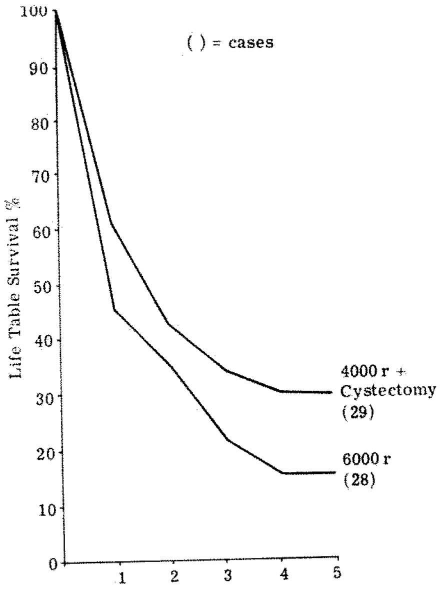
Conclusions

Planned preoperative irradiation combined with radical cystectomy appears to give improved 3- and 5-year results for T_3 bladder cancer, especially in patients showing an initial good response to irradiation.

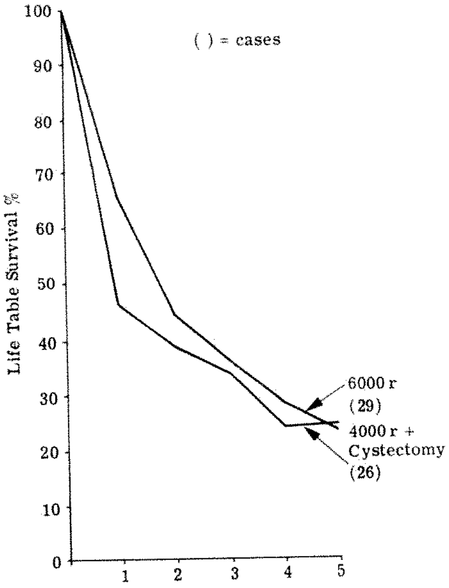
The unusually low incidence of metastatic nodes, especially in "down-staged" cases, suggests that this treatment destroys regional tumour spread, making radical operation safer and more successful.



⑦



⑧



⑨

Fig. 7. Survival by protocol treatment and age: under 60 years.

Fig. 8. Survival by protocol treatment and age: 60-64 years.

Fig. 9. Survival by protocol treatment and age: 65-70 years.

Our own lines of research are now directed towards finding effective radiosensitising and cytotoxic agents with which to try and increase the incidence and degree of tumour "down-staging" following preoperative irradiation.

It is hoped that this will improve further the results of combined modality treatment of deeply infiltrating bladder cancer which surely represents one of the greatest therapeutic challenges in the whole field of urological cancer.

Summary

The preliminary results are presented of a multicentre, co-operative randomised trial, sponsored by the Institute of Urology, London, in which radical irradiation (6,000 rads in 6 weeks) is compared with preoperative irradiation (4,000 rads in 4 weeks) plus radical cystectomy for deeply infiltrating carcinoma of the bladder (Stage T_3 or B_2C).

189 of the 199 cases entered into the trial between 1966 and 1975 were eligible for study. The overall 3- and 5-year survival rates for the combined treatment were 41% and 33%, respectively, compared with 28% and 21% for radical radiotherapy. The operative mortality was 7·8%. The difference between the two treatments in favour of the combined treatment has not yet reached the generally accepted level of significance ($P < 0{\cdot}05$), the p factors for the 3- and 5-year results being 0·064 and 0·077, respectively.

Of patients receiving the protocol combined treatment, reduction in tumour stage was found in the surgical specimen in 47% of cases. The overall incidence of nodal metastases was 23% (against the usual figure of 40-50%), and in the presence of a good response of the primary tumour to irradiation, only 8%. The 3- and 5-year survival rates for the down-staged cases were 66% and 55%, respectively, compared with 29% and 22% for patients showing no stage reduction in the surgical specimen.

The aim of our future studies is to find effective radiosensitising and cytotoxic agents with which to try and increase the incidence and degree of tumour response to pre-operative irradiation in the combined modality treatment of T_3 bladder cancers.

We should like to acknowledge the considerable assistance given by Mr Brian Shepherd and Mr Alan Turner, past and present senior urological registrars at the Royal Marsden Hospital, and also our research assistants, Dr M. Hossain and Dr S. Morris in assembling and analysing the collective data from the 8 centres. Our gratitude is due to Mr Peter Payne, Director of the South Metropolitan Cancer Registry, for statistical advice and computer facilities.

References

Bloom, H. J. G. (1971). Recent advances in radiotherapy of carcinoma of the bladder. Proceedings of the 10th International Cancer Congress, Houston, May 1970. *Oncology*, **3**, 234-250.

Hall, R. R., Bloom, H. J. G., Freeman, J. E., Nawrocki, A. and Wallace, D. M. (1974). Methotrexate treatment for advanced bladder cancer. *British Journal of Urology*, **46**, 431-438.

The Authors

D. M. Wallace OBE, M.S., FRCS, Emeritus Consultant Urologist (now Professor of Urology, University of Riyadh, Saudi Arabia).

H. J. G. Bloom, FRCP, FRCR, FACR, Consultant in Radiotherapy and Oncology.

Requests for reprints to: Dr H. J. G. Bloom, The Royal Marsden Hospital, Fulham Road, London, SW3.

British Journal of Urology (1976), **48**, 595-601 ©

Radiotherapy in the Treatment of Recurrent Bladder Cancer

W. D. RIDER and D. H. EVANS
Ontario Cancer Institute, Princess Margaret Hospital, Toronto, Canada

Although cancer of the bladder is the second most common tumour in urology, management is far from standardised and generates much controversy. Most publications have been reports on surgical or radiotherapeutic experience, and more recently combinations of these 2 methods.

We have been unable to find a comparable experience of radiotherapy in an "unplanned milieu".

The Ontario Cancer Institute (O.C.I.) is a radiotherapy referral centre serving a population of over 4·0 million people. Within this area, which includes about one-half of the province of Ontario there are almost as many surgical philosophies as there are urologists. Thus the vast majority of patients referred to the O.C.I. have had something more than a biopsy, usually several transurethral resections or a partial, or total cystectomy and sometimes chemotherapy.

Table I

Bladder Cancer O.C.I. 1958-1972

Transitional cell	1518
Squamous cell	51
Adenocarcinoma	20
Sarcoma	7
Ca. N.O.S.	25
Clinical	36
Total number	1657

Table II

TCC—T-stage

T-stage	No. of Patients
I	225
II	197
III	331
IV	179
IVA	40
IVB	197
X	319
Total	1518

Only the "late" stage cases arrive with only a biopsy. Thus the spectrum of preradiation therapy is wide.

During the years under review the radiotherapeutic philosophy has changed from one of "bladder only" treatment to a wide field irradiation designated to cover not only the bladder but also the regional lymphatic fields.

Methods and Materials

1,657 consecutive patients registered at the O.C.I. between 1958 and 1972 were reviewed retrospectively. Tumour classification as described by the U.I.C.C. (T.N.M.) staging has been assigned

Read at the 32nd Annual Meeting of the British Association of Urological Surgeons in London, June 1976.

Table III

TCC—Planned Treatment

Planned treatment	No. of patients	Percentage
Radical	554	36
Palliative	602	40
Not known	146	10
Not applicable (not treated)	216	14
Total	1518	–

wherever possible at the time of registration. During the past decade or more the majority of patients have been cystoscoped and examined under anaesthesia by the radiation oncologist and one of our consulting urologists at the O.C.I. Prior to the last decade a few patients were so assessed, but usually an estimate of "Stage" was based on data supplied by the referring urologist. It is quite clear that this "staging" is incorrect by the U.I.C.C. rules in the majority of instances, but nevertheless it has been used in an effort to assess the spectrum of disease as it reaches us.

Table I
Histological Classification

Since the transitional cell carcinomas account for 92% of the patients in this group they will be dealt with in detail alone.

Sex ratio: there were 1,117 males and 401 females in this group M:F = 2·81:1. The median age for males was 67·7 and 70·3 for females with a median for the group of 68·3 years.

Table II
Number of Patients in Allotted "T" Stages

Table III
Classification by Treatment

The definition of radical radiotherapy in this context is treatment given to eradicate local pelvic disease in the absence of detectable metastatic disease in patients considered medically fit for such treatment. All other treatment is considered to be palliative.

Table IV

All TCC—Status of Disease

Disease status	Alive	Dead
Well N.E.D.	217	16
Local disease	21	391
Distant disease	5	530
Other disease	–	289
Not known	2	47
Total	245	1273

Table V

All TCC Radically Treated Status of Disease

Disease status	Alive	Dead
Well N.E.D.	113	9
Local disease	9	119
Distant disease	4	164
Other disease	–	119
Not known	–	17
Total	126	428

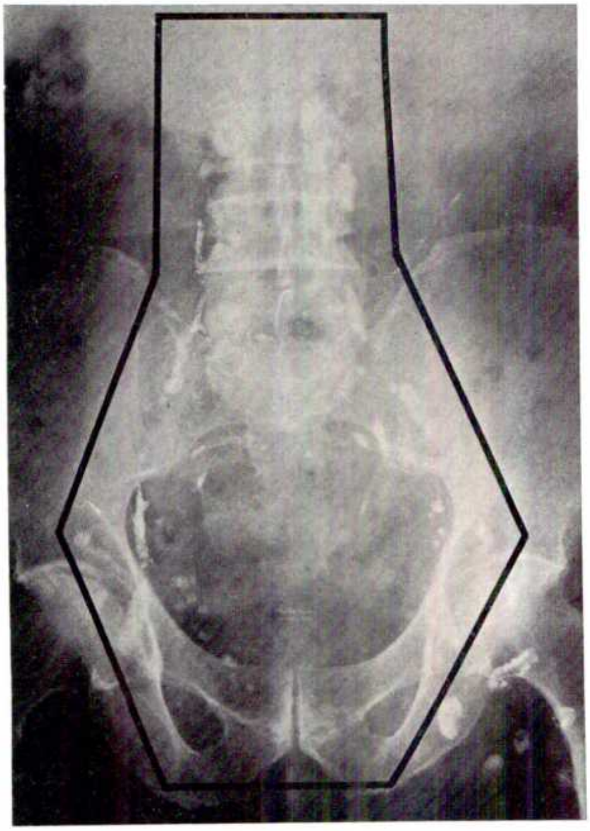


Fig. 1. Radiation field for radical treatment.

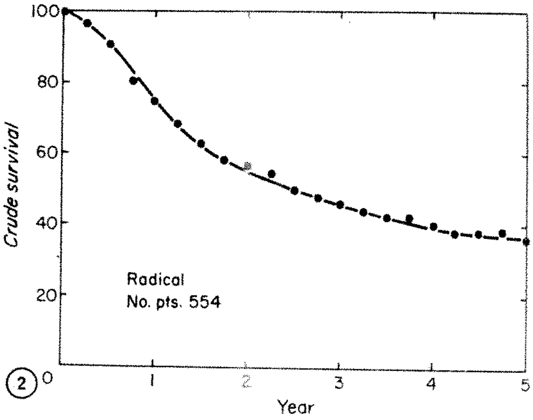
The present field used in the radical treatment is shown in Figure 1; it encompasses the bladder and its regional nodal drainage including the lower para-aortic nodes to L2. This field is treated to 3,500 rads in 16 fractions over 3 weeks with opposed fields. The bladder itself receives an additional 1,500 rads in 5 fractions in 1 week given through opposed fields or in a 360 degree rotational field. All treatment has been by supervoltage irradiation either Co60 or MEV X-rays.

There were 65 patients in this group who were treated with intracavitary colloidal gold for multiple superficial tumours.

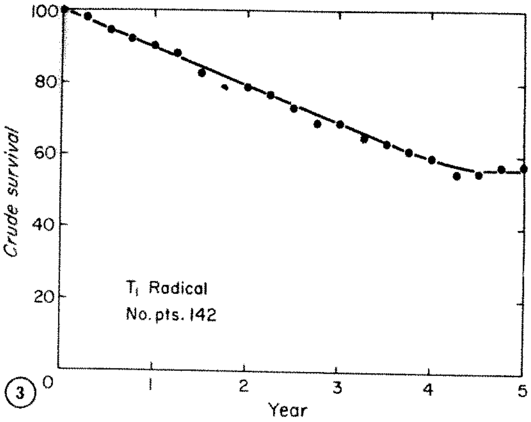
The palliatively treated patients were treated mainly on the 22 MEV Betatron and a few with the Co60 unit.

Results (Tables IV and V, Figs. 2-7)

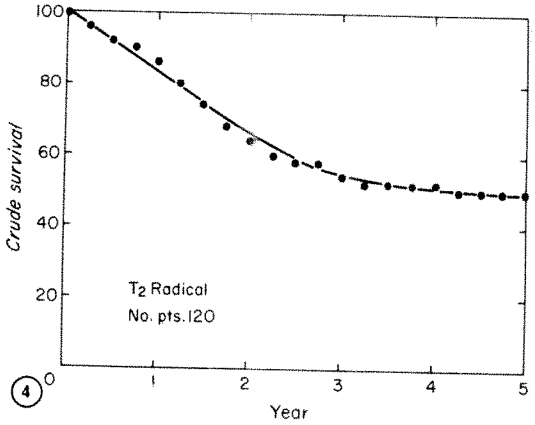
These results show good 5-year survival and comparable with other series using radiotherapy in T1 and T2 lesions realising that we cannot really match the series. The same applies to the surgical results. In the T3 group our results are poor in comparison with other published series. In comparing both the radical and palliative groups of T3 we find the results are comparable (Table VI). This probably reflects 2 factors, (1) understaging; (2) a presence of distant micro metastasis at the time of treatment, as both groups were dying of metastatic disease with the same incidence in spite of the differences in the treatment given. The results for the T3 lesions are comparable with the surgical results. In the T4 group the results are better than for T3.



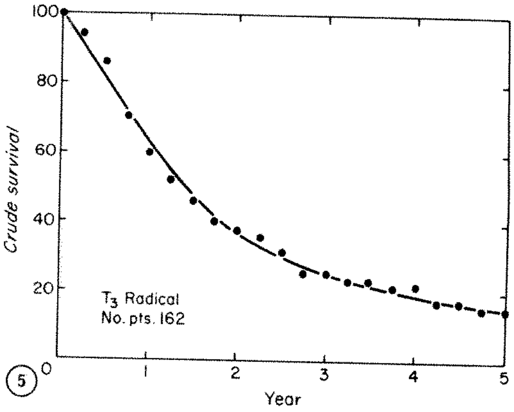
②



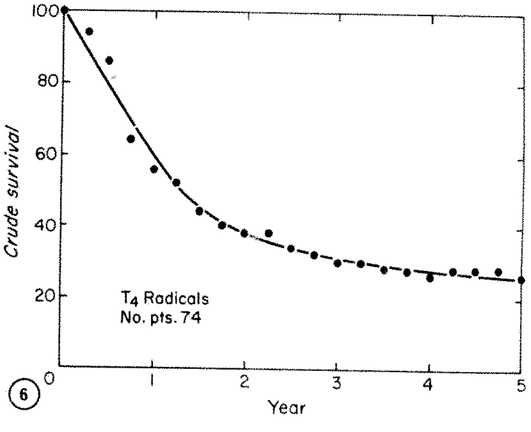
③



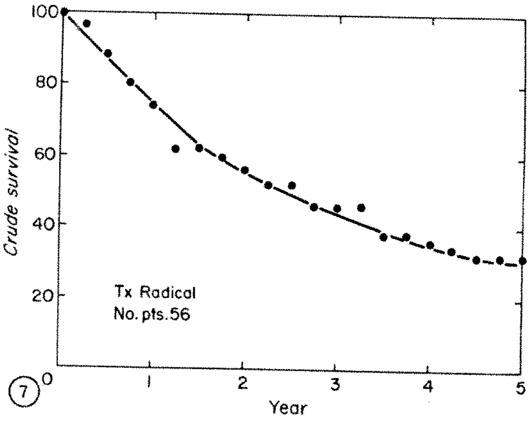
④



⑤



⑥



⑦

Fig. 2. Results of radical treatment in 554 patients: all stages.

Fig. 3. Results of medical treatment in 142 patients: T1.

Fig. 4. Results of medical treatment in 120 patients: T2.

Fig. 5. Results of medical treatment in 162 patients: T3.

Fig. 6. Results of medical treatment in 74 patients: T4.

Fig. 7. Results of medical treatment in 56 patients: TX.

Table VI

TCC—Disease Status at last Follow-up by T-stage and by Planned Treatment

Disease status at last follow-up	T2		T3	
	Radical	Palliative	Radical	Palliative
Alive				
Well	34	4	21	13
Local disease	1	1	2	–
Distant disease	1	–	1	–
Other disease	–	–	–	–
Disease status not known	–	–	–	1
Dead				
No disease	3	–	1	1
Local disease	22	11	42	32
Distant disease	30	9	61	41
Other disease	25	23	34	25
Disease status not known	4	–	–	3
Total	120	48	162	116

This may represent to some degree an element of understaging but it also represents a difference between the T4A and T4B category of lesions, with 12·1% and 6·5% 5-year survival respectively.

As time progresses so treatment changes and to evaluate these changes we compared the status of 2 groups of patients at 3-year post-treatment, the two groups were patients treated in 1958 and 1959 and 1970 and 1971. These results are noted in Figure 8.

The main difference in the 2 groups are: (1) the increase in control of local disease in the 1970-71 group, (2) the increase in the incidence of development of distant metastases and (3) the relative rise in patients dying of other causes. We feel that this represents a change in the treatment from local bladder radiation to the now adopted regional irradiation.

In assessing treatment failures, further treatment was carried out in 184 of the 554 radically treated patients. (Table VII) In analysing the total cystectomies done in both radical and palliative groups we found that 63 were for recurrent disease at a median time interval from treatment of 18·4 months. In the case of residual disease the cystectomies were done in 21 cases at a median time interval of 2·8 months. The survival of these patients is 43% at 5 years after surgery.

In cases of multiple superficial tumours unsuitable for transurethral resection, intravesical radioactive colloidal gold was used. In the 65 cases the calculated bladder dose was from 2,000 to 6,000 rads in 1 to 3 treatments. The total dose given was 6,000 rads and was brought up with external Co60 beam starting 2 to 4 weeks after the instillation of the gold. Of these 65 patients 38 out of 57 are alive and well at 5 years. In this group of patients there were 19 radical cystectomies done for recurrent and residual disease in 18 cases and only 1 for radiation fibrosis causing a small capacity bladder. The time interval to cystectomy varied from 6 months to 10 years from treatment.

One group of 82 patients was treated with radical radiation given as a small volume, *i.e.*, 6 × 6 cm in a 360 degree rotational field given as a single dose of 2,000 or 2,250 rads. This particular group of patients had a mean age of 80 years and were not considered medically fit to withstand a long course of radical radiation. Their median survival was 1 year but 9 out of 65 patients were alive at 5 years. The initial results were encouraging but the overall results were not good and this method of treatment is now used only in very specific cases.

Palliative Treatment

As previously indicated this group covers all other radiation therapy and accounts for 602 cases. The results are seen in Table VIII and indicate the severity of the disease as shown by the median survival figures.

Discussion

One of the axioms of cancer management, in general, is that the first planned attack should be designed for cure. Failure rates increase proportional to the number of previous attempts.

In spite of the fact that our case material was largely recurrent bladder cancer, it has been shown that an appreciable salvage can be attained by supervoltage irradiation and that the addition of regional lymph node irradiation has contributed mainly to this gain.

We have identified a high risk group who succumb to distant metastases, namely the Stage T3 patients. In this group the addition of regional lymph node irradiation has not improved survival; the pattern of failure suggests that these patients had "occult metastases" at the time of irradiation.

The corollary is that patients with T3 disease require some form of "adjunctive therapy" in an attempt to deal with micrometastases along the lines currently being advocated and practised in many other malignant conditions. At the moment there is no chemotherapeutic agent that can be recommended for such "adjunctive therapy".

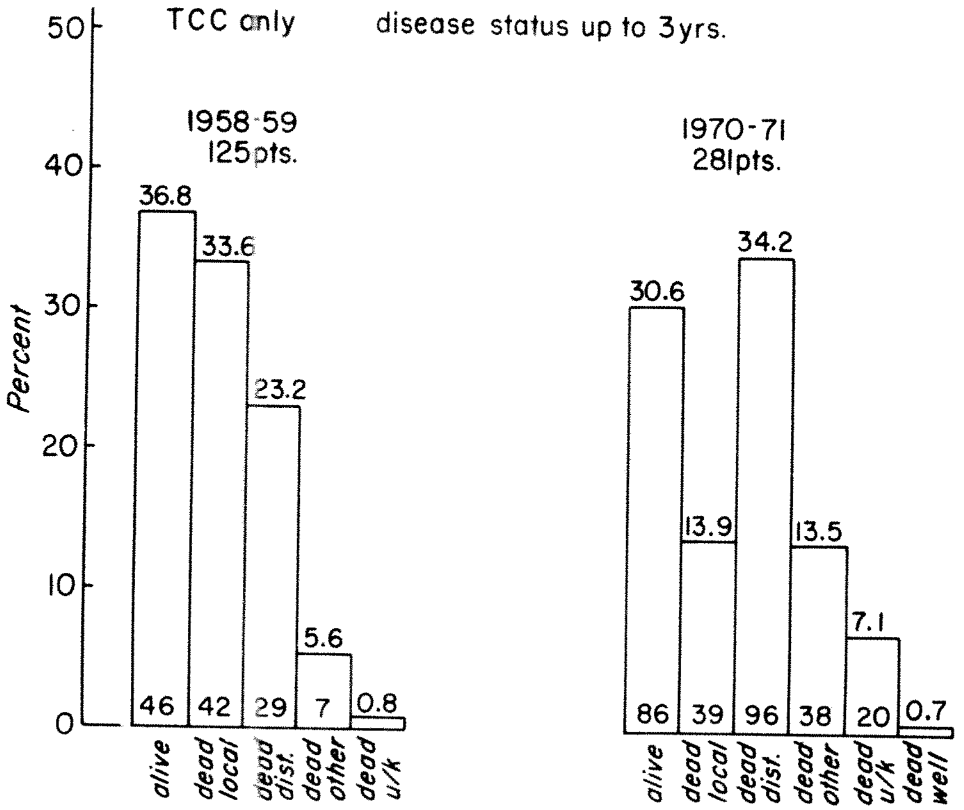


Fig. 8. Comparison of results for treatment of transitional cell bladder cancer between 1958-59 and 1970-71.

Table VII

TCC Radically Treated with Subsequent Treatment

T.U.R.	67
Cystectomy—Total	62
Partial	8
Urinary diversion	26
Radiation	10
Chemotherapy	8
Colostomy	2
Bowel resection	1
No subsequent treatment	375
Total	559

Table VIII

Palliative Treatment

Stage	Total No.	Alive at 5 years	Median survival (yrs)
T_1	33	3/25	1·25
T_2	48	3/37	1·1
T_3	116	13/74	0·9
T_4	284	8/201	0·5
T_x	121	4/91	0·4
	602		

It follows from the above that preoperative irradiation directed to the bladder alone or to the regional lymphatics as well, is doomed to failure because of occult distant metastases; it could, however, play a part in the Stage T2 cases provided the regional lymphatics are included in the treatment volume.

Summary

A retrospective review of 1,518 cases of transitional cell carcinoma treated by supervoltage irradiation is presented. The majority of patients had recurrent disease after previous treatment.

An appreciable salvage rate has been achieved.

A "high risk" group for distant metastases has been identified (T3) and the suggestion is made that adjunctive therapy be employed to deal with occult metastases.

The place of preoperative irradiation in Stage T2 tumours has been referred to.

It is recognised that this is an ageing population. Many die not of their cancer but from other causes.

It is difficult to compare these results with others published because of problems in selection and differences in staging the tumours.

We wish to thank the numerous consulting urologists who have assisted in evaluating these patients. We thank also Miss Teresa Chua and Dr DeBoer for the statistical help.

This study was done with a grant from the Ontario Cancer Foundation.

The Authors

W. D. Rider, FRCP(C), FRCR, Chief Radiation Oncologist.
D. H. Evans, MB, BS, Surgical Oncology Fellow.

Requests for reprints to be sent to Dr W. D. Rider, Princess Margaret Hospital, 500 Sherbourne Street, Toronto, Canada, M4X 1K9

British Journal of Urology (1976), **48**, 603-608 ©

Hyperthermia in the Treatment of Bladder Tumours

R. R. HALL, V. WADEHRA, J. M. TOWLER, J. R. HINDMARSH and P. O. BYRNE
Newcastle General Hospital, Newcastle upon Tyne

Hyperthermic irrigation of the urinary bladder at 80°C for 10 to 15 minutes was suggested by England *et al.* (1976) as it "may be preferable to cystectomy in certain poor-risk patients, or in those who refuse cystectomy for fear of impotence". Linke (1975) had previously used a similar method in 2 patients and had caused total necrosis of the bladder. We have now used this treatment in 4 patients but cannot recommend it for several reasons.

Patients

High temperature bladder irrigation was employed in 4 men aged 72 to 78 years as an alternative to cystectomy because of their age and frailty. 3 had T3 carcinoma of the bladder with troublesome haematuria or contracted bladders following previous radiotherapy. 1 had widespread urothelial atypia with scattered *in situ* changes in a contracted bladder with a uretero-ileal and an ileo-vesical fistula following radiotherapy 18 years previously.

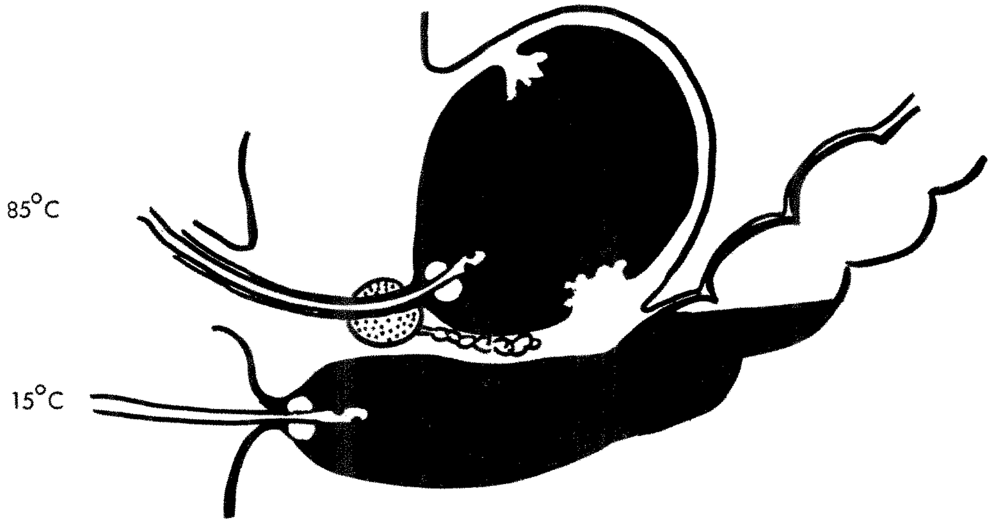


Fig. 1. Diagram to show hyperthermic irrigation of distended bladder. With protection of the rectum by separate irrigation with cold saline.

Read at the 32nd Annual Meeting of the British Association of Urological Surgeons in London, June 1976.

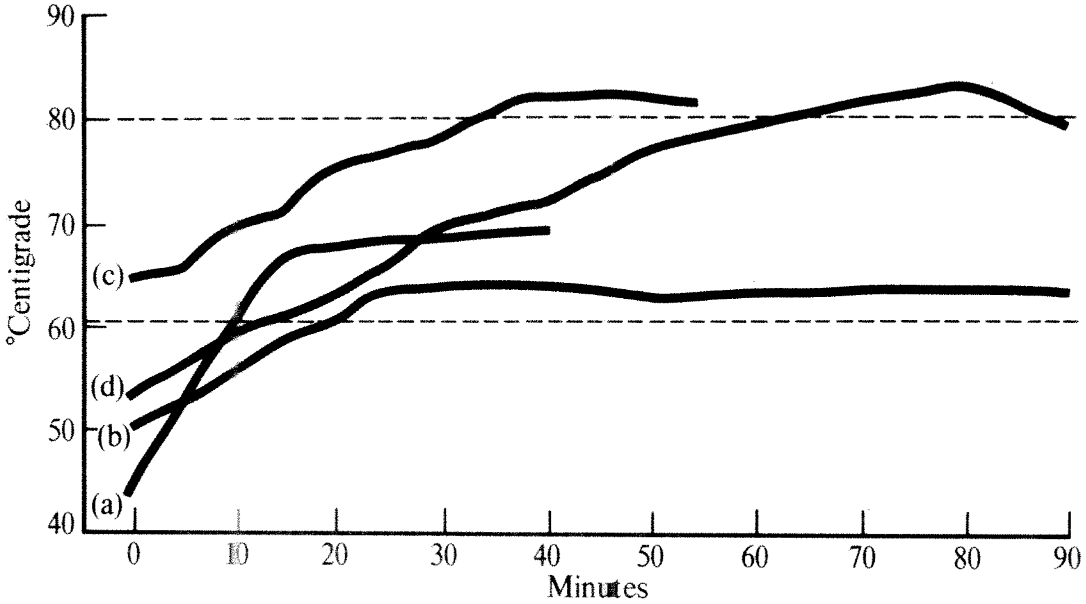


Fig. 2. Graph to show the intravesical temperature and duration of bladder irrigation during hyperthermia treatment.

Method (Fig. 1)

The bladder was irrigated with normal saline by a closed circuit system[1] incorporating a reservoir, peristaltic pump, filter, heater and 3-way irrigating Foley catheter. The bladder was distended to capacity where contracted, and to 200 to 300 ml where normal. A second Foley catheter was placed in the rectum so that the latter might be irrigated with cold saline if the temperature rose in the anterior rectal wall. This precaution was taken to avoid the possibility of producing a recto-vesical fistula by thermal necrosis.

The temperature of the irrigating fluid was measured at the inflow to and outflow from the Foley catheter. The temperature within the bladder and rectum and the thermal gradient across the bladder wall were measured by needle thermocouples placed at laparotomy in the bladder lumen, beneath the peritoneum covering the dome of the bladder and beneath the mucosa of the anterior rectal wall.

The bladder was isolated from the other viscera by a dry pack pushed well into the recto-vesical fossa which was then covered by aluminium foil. Bladder heating was maintained for 25 to 70 minutes while ileal conduit diversion of the urine was performed.

The duration and temperature of the irrigation is shown in Figure 2. It should be noted that in both patients irrigated above 80°C the period of irrigation was longer than that employed by England *et al.* (1976) and Linke (1975).

Results

Patient A (67°C for 25 minutes). When cystoscoped 3 months following treatment the bladder had contracted from 100 ml to 30 ml but was lined by normal urothelium (Fig. 3) instead of the atypia and *in situ* change present prior to treatment. No new tumour has developed during 1 year's cystoscopic follow-up. The urethra remains entirely normal.

---

[1] Patent applied for 1st August 1975.

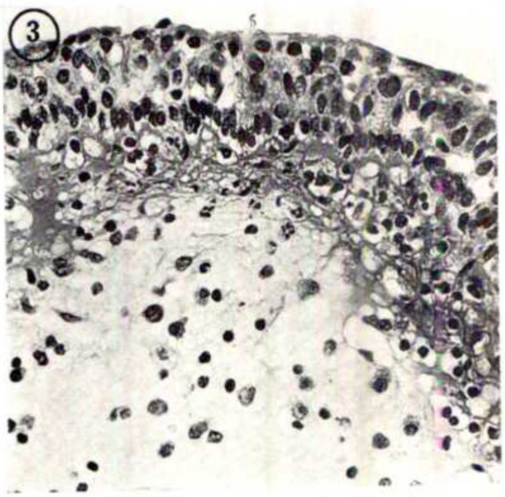


Fig. 3. Normal urothelium present in bladder of patient "A" 3 months following hyperthermic irrigation at 67°C for 25 minutes.

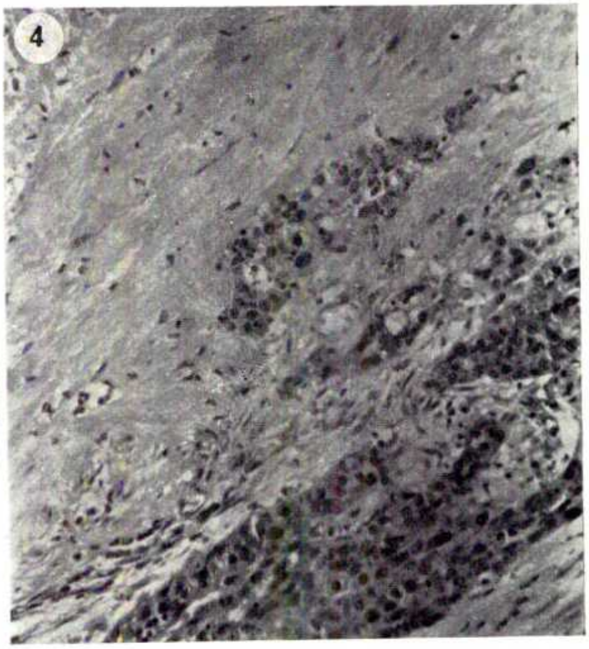
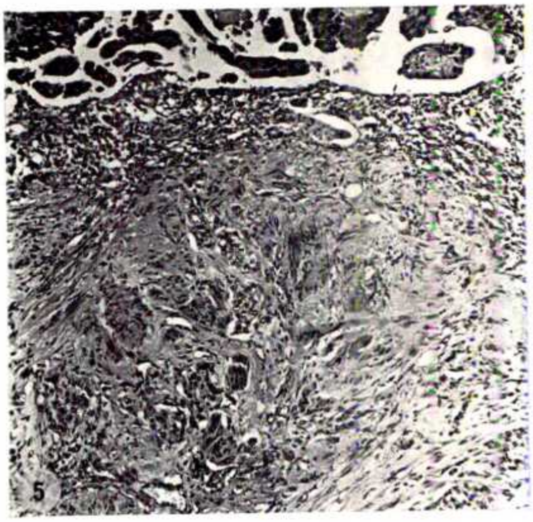


Fig. 4. Superficial necrosis of bladder with persistence of tumour and normal muscle in deeper layers of bladder wall 6½ months following hyperthermic irrigation at 63°C for 70 minutes (patient "B").



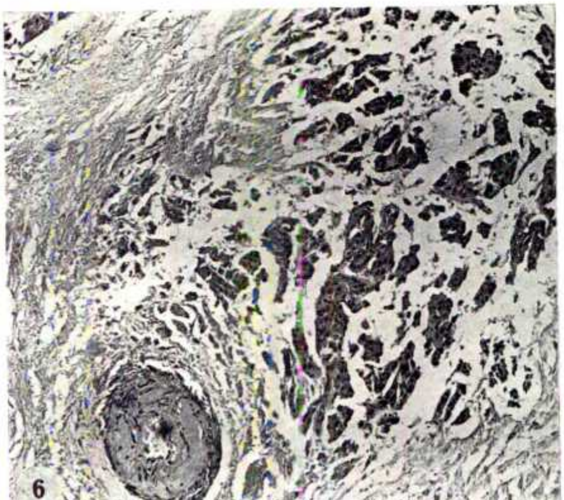


Fig. 5. Papillary transitional cell carcinoma infiltrating deep muscle, 5 months following hyperthermic irrigation at 82°C for 20 minutes (patient "C").

Fig. 6. Viable tumour surrounded by necrotic tissue in bladder that underwent full-thickness necrosis 6 weeks following irrigation at 82°C for 25 minutes (patient "D").

Patient B (63°C for 70 minutes). At 1 and 2 months following hyperthermia the patient complained of the sensation of fullness in a "phantom" bladder. By 3 months the bladder was palpable and suprapubic needle aspiration yielded 100 ml of serosanguinous fluid. The membranous urethra was obstructed by an impassable stricture. Subsequently, the bladder filled up again and caused discomfort leading to salvage cystectomy 6½ months following hyperthermia.

Histological examination of the operative specimen revealed that considerable superficial necrosis of the muscle had occurred and that there was no recognisable urothelium in the bladder, although the urothelium of the prostatic urethra was normal. Beneath the superficial necrosis, extensive poorly differentiated carcinoma persisted in the deep muscle of the bladder wall (Fig. 4). This patient died subsequently of pulmonary metastases.

Patient C (65° to 80°C for 35 minutes plus 82°C for 20 minutes). Cystoscopy 3 months following treatment revealed that the bladder, which had been of normal capacity previously, had contracted to a capacity of only 60 ml. However, persistent papillary tumour was also present and salvage cystectomy was performed 5 months following hyperthermia. Histological examination revealed papillary transitional cell carcinoma infiltrating the bladder wall, where extensive, but patchy, necrosis surrounded areas of viable muscle and tumour (Fig. 5).

Patient D (65° to 80°C for 40 minutes, plus 82°C for 25 minutes). Within a few days of operation it was clear that this patient had developed thrombosis of the corpus cavernosum with necrosis of the left shaft of the penis and overlying skin. Otherwise his recovery was uneventful until he suddenly deteriorated and died of generalised peritonitis 6 weeks following treatment.

Post mortem revealed necrosis and perforation of a 2 cm area of the anterior wall of the rectum 6 cm above the recto-vesical reflection. As no other cause was apparent it was presumed that this necrosis was due to thermal damage, the heated bladder having lain in contact with the upper rectum at this point despite precautions taken at the time of operation, and including irrigation of the lower rectum with cold saline during hyperthermia.

Histological examination of the bladder revealed necrosis of the full thickness of its muscle wall, but there were patches of viable tumour and muscle in the superficial muscle layers (Fig 6).

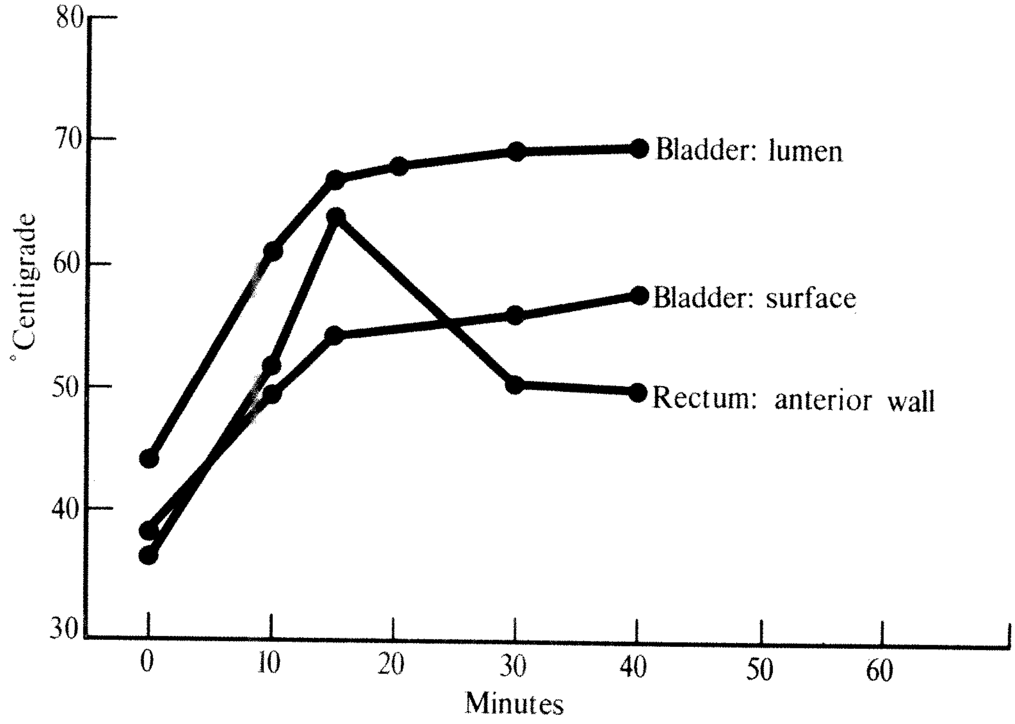


Fig. 7. Temperature difference between lumen and peritoneal surface of bladder during hyperthermic irrigation. Note comparable rise in temperature of anterior wall of rectum and subsequent fall following cold irrigation of rectum.

Table I

Case No.	Sex	Age	Remarks	Temp.	Time	Results
Contracted bladder and TIS tumour						
A	M	72	Contracted bladder 100 ml. TIS uretero-ileal plus ileovesical fistulae. Previous 4,000 rads	67°C	25 min.	Bladder capacity 30 ml. Normal urothelium
T3 tumour alternative to cystectomy						
B	M	76	T3 tumour. Contracted bladder. Previous 4,500 rads	63°C	70 min.	Salvage cystectomy. Persistent P3 tumour
C	M	87	T3 tumour. Haematuria	82°C 65°-80°C	20 min. 35 min.	Salvage cystectomy. Persistent P3 tumour
D	M	74	T3 tumour. Haematuria. Previous 6,000 rads	82°C 65°-80°C	25 min. 40 min.	Died 6 weeks post op. Necrosis anterior wall of rectum. Viable tumour amongst necrotic bladder muscle

Discussion

In all these cases the gross contracture of the bladders, the macroscopic appearance of the cystectomy specimen and subsequent histology provided clear evidence of extensive thermal necrosis within the bladder wall. However, in 3 cases there was equally clear evidence that hyperthermia, even to 82°C for 25 minutes, does not necessarily destroy transitional cell carcinoma within the bladder wall.

It is true that the outer surface of the bladder was at a lower temperature than that irrigating the bladder lumen. Recordings taken from the first patient (Fig. 7) demonstrate a thermal gradient across the bladder wall of approximately 15°C, together with comparable heating of the anterior wall of the rectum. Similar thermal gradients were found in the other 3 patients. Thus tumour within the deep muscle of the bladder would have been heated to a lesser degree than that at the mucosal surface, but this cannot be the whole explanation for apparently viable tumour cells were found 6 weeks following hyperthermia in the midst of dead muscle and viable tumour and muscle was found superficially in some areas with necrotic muscle beyond, where the temperature would have been lower.

Furthermore, the necrosis induced in the rectum of patient D illustrates the ability of the lowest bladder wall temperature to destroy normal tissues.

Summary

High temperature bladder irrigation was employed in 4 men as an alternative to cystectomy because of their age and frailty.

Hyperthermic irrigation of the bladder from 63°C for 70 minutes to 82°C for 25 minutes caused partial, but not total, necrosis of the bladder.

Transitional cell carcinoma appears to be resistant *in vivo*, in some cases, to heating at temperatures that destroy adjacent normal structures.

Hyperthermic irrigation of the bladder at these high temperatures may be hazardous.

In view of these findings we cannot recommend high temperature bladder irrigation as an alternative to cystectomy even in poor risk patients.

References

England, H. R., Anderson, J. D., Minasian, H., Marshall, V. R., Molland, E. A. and Blandy, J. P. (1975). The therapeutic application of hyperthermia in the bladder. *British Journal of Urology*, **47**, 849-852.

Linke, C. (1975). Personal communication.

The Authors

R. R. Hall, FRCS, Consultant Urologist.
V. Wadehra, MB, BS, Senior Registrar, Department of Pathology.
J. M. Towler, FRCS, Urological Registrar (now Senior Registrar, Department of Urology, Aberdeen Royal Infirmary).
J. R. Hindmarsh, FRCS, Urological Registrar.
P. O. Byrne, BSc, Senior Physicist, Department of Medical Physics.

British Journal of Urology (1976), **48**, 609-615 ©

Treatment of Advanced Bladder Cancer with Adriamycin and 5-Fluorouracil

R. J. CROSS, R. W. GLASHAN, C. S. HUMPHREY, M. R. G. ROBINSON, P. H. SMITH and R. E. WILLIAMS

The Yorkshire Urological Cancer Research Group, Pontefract General Infirmary, Pontefract, Huddersfield Royal Infirmary, Huddersfield, and Leeds (St James's) University Hospital, Leeds.

The results of the conventional management of invasive bladder cancer by cystectomy and radiotherapy alone or in combination are unacceptable. Jewett's review of the literature (1970) showed 5-year survival figures after cystectomy of 16 to 28% when the tumour had spread deeply into the bladder wall and 9 to 18% if invasion of the perivesical fat had occurred. In the presence of metastatic disease only 3% of the patients survived for 5 years. Similarly disappointing results are achieved by radiotherapy (Cuccia, 1969; Edsmyr, 1975).

The failure of local treatment in the majority of patients with invasive bladder cancer casts doubt upon conventional methods of clinical assessment and suggests that the disease is widespread, in microscopical if not macroscopical form, at the time of presentation. If this concept is accepted the need for additional systemic treatment is evident, and it was with this objective in mind that we began to study the use of cytotoxic drugs in patients with advanced bladder cancer.

Patients and Methods

24 patients with histologically proven transitional cell bladder tumours were entered into the study. Using the UICC classification of tumours (UICC, 1974), 14 of the patients were regarded as having T4 bladder tumours, and 8 patients as T3 tumours. One patient had a T1 tumour, but was included in the series because of the presence of lung and skin metastases (the latter positive on biopsy), and 1 patient presented with distant metastases after a previous cystectomy. Details of the patients are given in Table I.

Only patients with advanced bladder tumours were eligible for the trial. Patients were excluded if their life expectancy was estimated to be less than 3 months, if they had serious intercurrent disease, or if their haematological status contraindicated cytotoxic therapy.

Before treatment all active infection was controlled and blood transfusion was given when indicated.

Assessment

Patients were assessed for their suitability for chemotherapy with adriamycin and 5-fluorouracil and for their response to treatment. Haemoglobin estimations, white cell and platelet counts, liver and renal function tests and electrocardiograms were performed before each treatment. The evaluation of the response to treatment was made on clinical history and physical examination, excretory urogram, cystoscopy and bi-manual examination of the pelvis under general anaesthesia, chest and skeletal radiography and isotopic bone scanning performed before and at 3-monthly

Read at the 32nd Annual Meeting of the British Association of Urological Surgeons in London, June 1976.

Table I

Details of 24 Patients with Bladder Cancer Undergoing Chemotherapy

Age	Sex	Previous treatment	Stage of tumour (TNM)	Site of metastases
48	M	None	T4	–
72	M	None	T4	–
72	M	None	T4	Bone
61	F	None	T3	–
66	M	HER (6/12)	T4	Bone
60	M	None	T4	–
58	M	HER (6/12)	T4	Lungs
71	M	HER (18/12)	T3	–
48	M	None	T3	–
54	M	None	T4	–
69	M	HER (3/12)	T4	–
57	F	None	T3	–
54	F	None	T4	Liver
61	M	None	T3	–
65	M	HER (12/12)	T4	Liver
57	M	None	T4	–
69	M	HER (12/12)	T3	Liver
61	M	None	T3	–
81	M	None	T1	Skin + lungs
52	M	HER (6/12)	T4	–
61	M	Cystectomy	–	Bone + lungs
55	M	HER (14/12)	T3	–
59	M	None	T4	Lungs
61	M	HER (6/12)	T4	–

* HER—Radiotherapy, which was radical in all cases. Figures denote time in months between completion of radiotherapy and start of chemotherapy.

intervals, during chemotherapy. Lymphangiography and liver scans were performed when clinically indicated.

Treatment Schedule

Adriamycin (50 mg/m^2) and 5-fluorouracil (500 mg/m^2) were given at 3-weekly intervals by injection into the side arm of a fast-running intravenous infusion of dextrose. The first injection was usually given whilst the patient was in hospital after the completion of the initial assessment. Thereafter treatment was given on an out-patient basis.

In the presence of marked bone marrow depression the 3-weekly interval was extended until such time as the white cell count had risen to more than 3,500/cmm and the platelet count to more than 100,000/cmm. If there was little haematological depression after 2 injections the dose of drugs was increased to 60 mg/m^2 and 600 mg/m^2 respectively. Drug dosage was reduced in patients with impaired liver function, by one-half if the serum bilirubin was between 1 and 3 mg/100 ml and by three-quarters if the concentration was greater than 3 mg/100 ml.

After 4 injections, if there was evidence of a response, or if tumour progression had been halted a further course of treatment was given up to a total dose of adriamycin of 500 mg/m^2. If the tumour progressed the therapy was regarded as having failed, and treatment was stopped.

Table II

Effect of Chemotherapy upon Symptoms due to Bladder Tumours in 20 Patients

Symptoms	Patients	Improvement
Haematuria	17	14 (83%)
Frequency and urgency*	14	9 (64%)
Pelvic pain	4	2 (50%)
Bone pain	3	3 (100%)
Poor appetite	8	6 (75%)

* Not associated with infection.

Evaluation

Following treatment and assessment the patients were classified as showing:

(*a*) Complete remission, indicating that the patient had neither signs nor symptoms of the original tumour.

(*b*) Partial remission, with a measurable reduction in the tumour bulk (either of the primary lesion or of a metastasis) without the appearance of new tumour.

(*c*) No change, signifying that although the patient might be symptomatically improved there had been no measurable reduction in size of the tumour (or evidence of progression).

(*d*) Progression, with progression of signs or symptoms.

In addition to recording the progress of the patients' individual symptoms, an estimate of their general health was made using the Karnofsky grading of performance status (Karnofsky, 1961).

Results

Of the 24 patients entering the study, 4 could not be assessed. Of these 3 died from their cancer before a second injection could be given and represent failures of selection; the fourth patient underwent cystectomy for intractable symptoms of a post-radiotherapy contracted bladder after only 1 injection.

Of the remaining 20 patients, 9 are alive between 7 and 17 months from the start of the treatment 11 patients have died from their disease at intervals of 3 to 12 months from the start of the treatment.

Objective Response

Objective evidence of a tumour response was seen in 7 patients (35%). This was complete in 3 and partial in 4 patients. 2 of the 3 patients who had a complete response are alive and are free from all evidence of the disease at intervals of 13 and 16 months. The third patient has extensive metastases in liver and lymph nodes, after remaining free of disease for 8 months. Of the 4 patients with a partial response 1 is free from symptoms on follow-up at 13 months and the initial reduction in tumour mass has been maintained. In the other 3 patients the partial response was only temporary (2, 4 and 9 months) and all have subsequently died from their disease. No patient showing a remission relapsed until the course of adriamycin had been completed.

In 4 patients, although there has been no objective reduction in tumour size, undoubted improvement in symptomatology has made the use of chemotherapy worthwhile. In each case the tumour has been held in check for periods of 4 to 6 months without any additional therapy.

Table III

Complications of Chemotherapy for Bladder Cancer in 20 Patients

Complication	Number of patients
Gastrointestinal	
Nausea	20
Vomiting	8 (1 severe)
Diarrhoea	3
Perianal soreness	10
Oral ulceration	5
Transient myelosuppression	20 (4 severe)
Ankle oedema	3
Hair loss	20
Cellulitis	3

The general health of 1 patient was improved to the extent that, previously having been thought to be unfit for any other form of treatment, she has undergone cystectomy. The other patients have received radiotherapy.

There was no obvious benefit from treatment in 9 patients who continued to deteriorate and who died from their disease.

Subjective Response

Table II shows the effect of adriamycin and 5-fluorouracil upon the symptoms produced by bladder tumours. Particularly impressive was the reduction or abolition of haematuria often within 2 weeks of the first injection, occurring even when there was no other evidence of response. Symptoms due to an irritable bladder, and pelvic and perineal pain were less frequently improved, although over one-half of the patients experienced some relief. Pain from metastases in bone was abolished in 1 patient and reduced in 2 others. Three-quarters of the patients with a previously poor appetite noted an improvement, and 11 gained in weight (average 5·1 kg). There was an improvement in performance status in 10 patients.

Complications of Treatment

The complications are listed in Table III. Gastrointestinal side-effects were common, but only 1 patient, who invariably vomited for up to 48 hours after each injection, was severely affected. Interestingly, although diarrhoea was infrequent, half the patients experienced perianal irritation or soreness. In some instances a redness of the perianal skin was observed. This was not associated with a fungal infection and no other cause could be found. 5 patients had transient oral ulceration. This required treatment only in 1 patient in whom there was an infection with *Candida albicans.*

The depression of white cell and platelet counts was predictable and almost invariably returned to normal levels in the 3-week interval between injections. 4 patients presented haematological problems. In 2 patients there was a profound depression of platelets and white cells with spontaneous recovery. In 1 of these cases, where impaired liver function may have been responsible for the marked marrow toxicity, a serious septicaemia developed. 2 further patients required blood transfusion to correct moderate degrees of anaemia which were presumed to be the result of the treatment as there were no obvious sources of blood loss.

Cardiotoxicity is a well-documented complication of adriamycin therapy (Lefrak *et al.*, 1973). In this series 3 patients developed transient ankle oedema, but without other evidence of congestive heart failure. Serial electrocardiographs during treatment revealed no abnormality.

Table IV

The Effect of Previous Radiotherapy, Degree of Tumour Differentiation and Patient "Fitness" on the Response of Bladder Carcinoma to Chemotherapy in 20 Patients

	No.	Objective response	Subjective response	Failure
*Previous treatment**				
Radiotherapy	7	3	–	4
None	12	3	4	5
*Tumour differentiation**				
Anaplastic	2	1	–	1
Poorly diff.	9	3	–	6
Well diff.	8	2	4	2
Performance status				
Karnofsky 70 or more	13	6	3	4
Karnofsky less than 70	7	1	1	5

* Excluding the patient previously treated by cystectomy.

Loss of hair from the head and other sites occurred in all patients and in many was total. The hair grew again in all patients when the adriamycin was stopped.

Cellulitis developed in the region of the infusion in 3 patients. In 2 this was minor but in the third an extensive area of forearm slough required surgical excision, emphasising the importance of preventing perivenous extravasation.

Discussion

The role of chemotherapy in the management of bladder cancer is not yet clear. Carter and Wasserman (1975) considered that only 3 drugs, mitomycin C, adriamycin and 5-fluorouracil had been adequately evaluated; all showed evidence of activity against transitional cell bladder cancer ranging from 25 to 35%. Although the evidence for activity of adriamycin comes largely from Phase I studies of the drug carried out on large numbers of patients with various advanced malignancies including patients with bladder cancer, response rates against bladder cancer of 30 to 35% were found by Middleman, Luce and Frei (1971), Bonadonna *et al.* (1972) and O'Bryan *et al.* (1973). However, Tan and his colleagues (1973) failed to find any evidence for activity of adriamycin in 5 patients with bladder cancer and Merrin *et al.* (1975) showed a response rate of 10%.

5-fluorouracil has been used to treat bladder cancer in a number of series, although many of them contain only small numbers of patients. Reviewing these Carter and Wasserman (1975) found an overall response rate for this drug of 26%. The evidence for activity of both these drugs when used as single agents prompted us to study the use of them in combination, hoping that we would find an additive effect. Our response rate of 35% is inconclusive and we shall seek to clarify the issue in a further trial. It is, however, noteworthy that no patient showing a remission relapsed whilst still on adriamycin.

Several factors may possibly influence the results of chemotherapy including the histological grade of the tumour, previous treatment and the general health of the patients (Table IV). 7 patients had undergone radiotherapy previously and presented with either recurrent or residual disease. Of these 7, 3 showed evidence of tumour remission (1 complete and 2 partial) and 4 showed progression of their tumours. 12 patients presented with advanced disease having had no previous treatment, and of these 3 responded to the chemotherapy (2 completely, 1 partially), 4 had a symptomatic response, and in the other 5 the tumour progressed. Although the numbers of patients are small, there would seem to be little difference between those who had undergone previous radiotherapy and those who had not. A similar conclusion comes from a study of the degree of histological differentiation of the tumour, poorly and well differentiated tumours behaving in a similar way to each other. However, the general health of the patient prior to treatment does appear to have had some bearing upon the outcome of chemotherapy. Thus of 7 patients with a performance status of less than 70 before treatment, 1 had an objective response, 1 had a symptomatic response whilst in 5 there was relentless progression of the tumour. On the other hand, of the 13 patients who had a performance status of 70 or more there were 6 objective responses, 3 subjective responses and only 4 failures.

The objective tumour response rate obtained in trials such as this is clearly of the utmost importance in helping to plan future strategy for the management of patients with malignant disease. From the patients' point of view the quality of life experienced whilst being treated is of even greater importance. Looked at from this aspect, we have no doubt that the use of adriamycin and 5-fluorouracil has been of benefit to most of these patients. Reference has already been made to the impressive relief of many of the symptoms; this has been observed even in some patients whose disease was otherwise progressing. The symptomatic relief, improvement in appetite and gain in weight usually far outweighed the side-effects of the treatment. In only 2 patients did we feel that the therapy was detrimental; 1 patient required surgery because of cellulitis and skin gangrene at the site of the infusion and 1 patient developed septicaemia which was probably the result of the marrow depression produced by the drugs.

In looking to the future it is relevant to observe that all the agents so far tested have shown some activity against bladder tumours suggesting that effective combination chemotherapy in this disease is a real possibility. The failure of a purely local attack to cure the majority of patients with invasive bladder cancer justifies the search for an effective and safe form of systemic therapy which can be included as an adjuvant to either radiotherapy or cystectomy in the potentially curable patient. The early experience in carcinoma of the breast with adjuvant chemotherapy and mastectomy (Fisher *et al.*, 1975) raises the hope that such an approach will result in an improved survival of patients with bladder cancer. For the time being, however, the urgent need is for studies of the many drugs not yet evaluated.

Summary

The cytotoxic drug combination of adriamycin and 5-fluorouracil has resulted in a 35% objective response in 20 patients with advanced bladder cancer. This has been achieved with minimal toxicity and on an out-patient basis.

If the survival rate of patients with invasive bladder cancer is to be improved it seems likely that some form of systemic treatment will need to be added to the local measures currently in use.

Further studies of different chemotherapeutic agents should help to define an effective and safe form of adjunvant therapy.

We should like to acknowledge the financial assistance given to us by the Yorkshire Regional Cancer Organisation without which this study would have been impossible. This work is part of a pilot study carried out by the E.O.R.T.C. Urological Group.

References

BONADONNA, G., MONFARDINI, S., DELENA, M., FOSSATI-BELLANI, F. and BERETTA, G. (1972). Clinical trials with adriamycin. In *International Symposium on Adriamycin*. New York: Springer, pp. 139-152.

CARTER, S. K. and WASSERMAN, T. H. (1975). The chemotherapy of urologic cancer. *Cancer*, **36**, 729-747.

CUCCIA, C. A., (1969). The radiation attack. *Journal of the American Medical Association*, 347-348.

EDSMYR, F. (1975). Radiotherapy in the management of bladder cancer. In *The Biology and Clinical Management of Bladder Cancer*, ed. E. H. Cooper and R. E. Williams. Oxford: Blackwell, pp. 229-254.

FISHER, B., CARBONE, P., ECONOMON, S. G., FRELICK, R., GLASS, A., LERNER, H., REDMOND, C., ZELEN, M., BAND, P., KATRYCH, D., WOLMARK, N. and FISHER, E. R. (1975). L-Phenylalanine mustard (L-PAM) in the management of primary breast cancer. *New England Journal of Medicine*, **292**, 117-122.

JEWETT, H. J. (1970). Treatment of carcinoma of the bladder: a summary. In *Sixth National Cancer Conference Proceedings*. Philadelphia: Lippincott, pp. 211-217.

KARNOFSKY, D. A. (1961). Meaningful clinical classification of therapeutic responses to anticancer drugs. *Clinical Pharmacology and Therapeutics*, **2**, 709-712.

LEFRAK, E. A., PITHA, J., ROSENHEIM, S. and GOTTLIEB, A. J. (1973). A clinicopathologic analysis of adriamycin cardiotoxicity. *Cancer*, **32**, 302-314.

MERRIN, C., CARTAGENA, R., WAJSMAN, Z., BAUMGARTNER, G. and MURPHY, G. P. (1975). Chemotherapy of bladder carcinoma with cyclophosphamide and adriamycin. *Journal of Urology*, **114**, 884-888).

MIDDLEMAN, E., LUCE, J. and FREI, E. (1971). Clinical trials with adriamycin. *Cancer*, **28**, 844-850.

O'BRYAN, R. M., LUCE, J. K., TALLEY, R. W., GOTTLIEB, J. A., BAKER, L. H. and BONADONNA, G. (1973). Phase II evaluation of adriamycin in human neoplasia. *Cancer*, **32**, 1-8.

TAN, C., ETCUBANAS, E., WOLLNER, N., ROSEN, G., GILLADOGA, A., SHOWEL, J., MURPHY, M. L. and KRAKOFF, I. H. (1973). Adriamycin—an antitumor antibiotic in the treatment of neoplastic diseases. *Cancer*, **32**, 9-17.

UNION INTERNATIONALE CONTRE LE CANCRUM. (1974). TNM classification of malignant tumours. 2nd ed. Geneva. pp. 79-82.

The Authors

R. J. Cross, MB, ChB, Clinical Assistant in Urology, Pontefract General Infirmary.
R. W. Glashan, FRCS, Consultant in Urology, Huddersfield Royal Infirmary.
C. S. Humphrey, FRCS, Lecturer in Surgery, Leeds (St James's) University Hospital.
M. R. G. Robinson, FRCS, Consultant in Urology, Pontefract General Infirmary.
P. H. Smith, FRCS, Consultant in Urology, Leeds (St James's) University Hospital.
R. E. Williams, MD, FRCS, Consultant in Urology, Leeds (St James's) University Hospital.

Requests for reprints to Mr P. H. Smith, at Leeds (St James's) University Hospital, Leeds.

British Journal of Urology (1976), **48**, 617-621 ©

The Endemic Bladder Stones of Indonesia—Epidemiology and Clinical Features

KAMARDI THALUT, AHMAD RIZAL, J. G. BROCKIS, R. C. BOWYER, T. A. TAYLOR and Z. S. WISNIEWSKI
Padang General Hospital, West Sumatra, Indonesia and Royal Perth Hospital, Perth, Western Australia

Bladder stones are common amongst young male children of the lower social and economic classes of the Indonesian rural population. As a joint Indonesian-Australian project, we have studied 87 children suffering from the condition.

Here we report our findings on the epidemiology and clinical features whilst a second paper provides details of biochemical investigations designed to disclose the basic cause of the condition.

The area selected for study was West Sumatra, which has a population of approximately 2½ million, stretching along the west coast of the island of Sumatra. Padang and Bukittingi hospitals serve the area. 200 new cases of children with bladder stones report to these hospitals each year, with an overall incidence of 8·3/100,000 population per year. Whilst the most populous area is the city of Padang, which is on the coast, very few patients come from there—the largest number are from Pariaman, a low-lying rice-growing rural area to the north

The geographical distribution of our patients is shown in Figure 1. The area, within a degree of the equator, is a low-lying coastal plain growing rice, behind which are high mountains with jungle. Bukittingi is a hill town with a moderate climate. Most of the affected children come from poor homes built on land adjoining streams from which the rice paddies are flooded.

The peak age of onset in our series is between 2 and 4 years (Fig. 2) and there is a ratio of 12:1 males to females (which compares with ratios of 20 males to 1 female in China and Syria (Thomson, 1921; Brown and Brown, 1941); 13:1 in India (Andersen, 1962) and 10:1 in Thailand (Halstead and Valyasevi, 1967). An investigation of the children's families shows that it is rare for more than 1 child to be affected, even though large families are the rule. The children are of average weight and height and do not show any external appearances of malnutrition. There is no association between the development of stones and kwashiorkor and no evidence of Vitamin A or D deficiency so far as we are able to determine.

The commonest clinical presentation is for a child to pull on his penis, which seems to help to initiate micturition and to relieve strangury. The sight of a child doing this is almost diagnostic! Other common symptoms are suprapubic pain and frequency of micturition. Retention of urine due to impaction of the stone is rare, and gross haematuria, as distinct from the presence of red cells in the urine is also infrequent. No child has been known to suffer from renal colic and the only renal symptoms that have occurred can be attributed to ureteric reflux and infection. 50 patients have had preoperative intravenous urograms: 8 showed bilateral urinary tract dilatation and 13 unilateral. Reflux was present in these children and postoperative X-rays taken much later have shown a trend to return to normality, suggesting an association with urinary tract infection.

Diarrhoea is common amongst young children in this tropical area. Whilst mothers of the affected children frequently mentioned this, it has proved impossible to show that there was a higher incidence in children with stone; it is also very difficult to measure the severity of diarrhoea attacks.

Read at the 32nd Annual Meeting of the British Association of Urological Surgeons in London, June 1976.

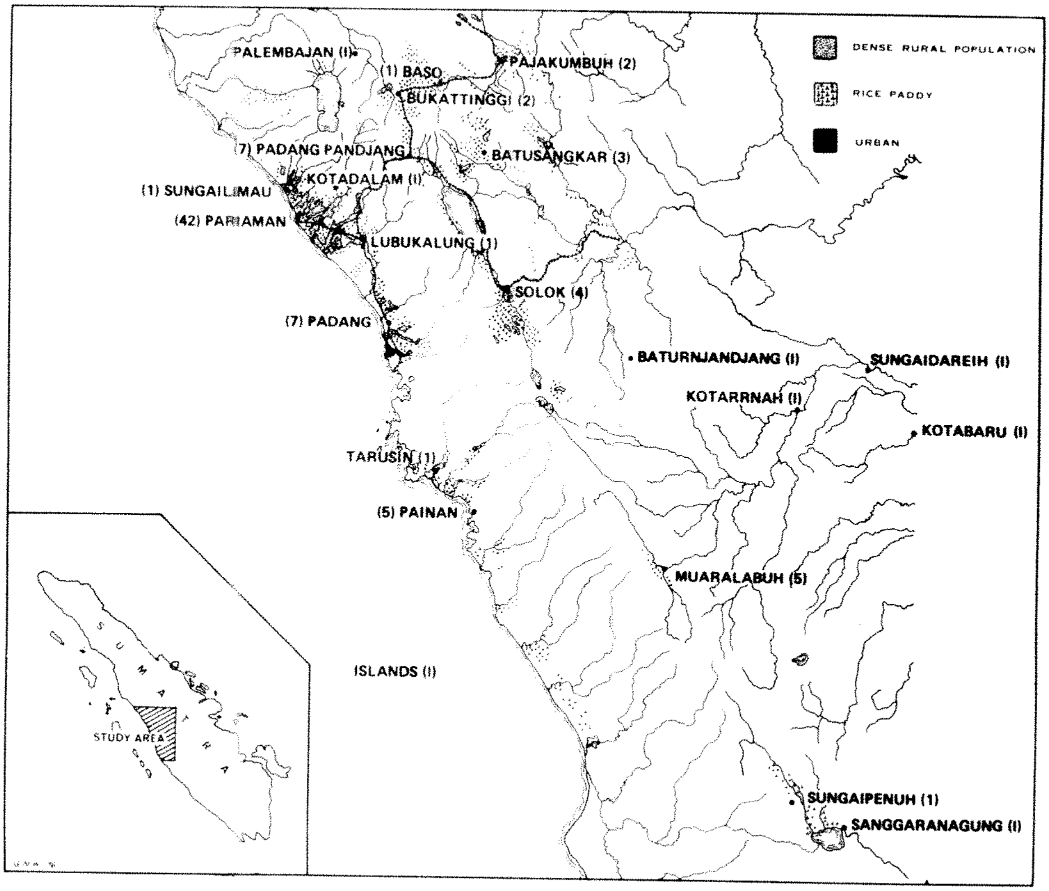


Fig. 1. Map of West Sumatra showing rural distribution of 87 patients.

Recurrence after removal of a stone is very rare, occurring only once in our series.

The diet of the children who come from a rural low socio-economic group is of breast milk supplemented by polished rice. They do not receive any dairy products and the only other source of protein is a minute amount of fish. For the younger children, the rice may be predigested in the mother's mouth. Thus almost the only source of protein is mother's milk or rice. This diet is also low in fat and in inorganic phosphate. Human milk, unlike cow's milk, does not have a high phosphate content.

The water supply in country areas is from shallow wells—the water level being that of the paddy fields. It is sometimes cleared by filtration through river sand, but often has a high bacterial count. Padang water supply is piped and chlorinated but does not reach all the inhabitants of the town and there are many wells in the suburbs.

Discussion

Endemic bladder stones were common in 18th- and 19th-century Europe. Civiale (1838) reported from France that 45% of 5,383 cases of stone occurred in children below the age of 20. William Cheselden (1723) of St Thomas's Hospital, London, operated upon 213 cases of bladder stone, of whom 102 were under the age of 10 years and another 50 between 10 and 20.

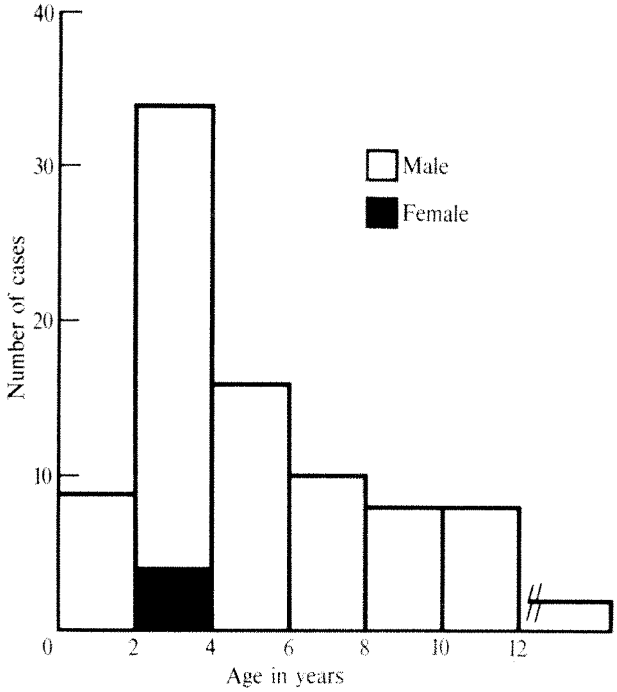


Fig. 2. Age and sex of 87 bladder stone patients.

Yelloly (1829) and Crosse (1835) reported from the Norfolk and Norwich Hospital, England, that endemic stones of childhood were very common in the eastern grain growing part of that county as compared with the west which had mixed farming.

Vesical calculus practically ceased to exist as an endemic disease in northern Europe between the years 1910 and 1930 (Lett, 1936; Thomas, 1949).

The condition still exists in a belt of countries beginning in southern Russia and the Balkans (Račić, 1935), passing through Egypt (Loutfi, Hamid *et al.*, 1972); Turkey (Eckstein, 1961); Israel (Levy and Falk, 1957); Lebanon/Syria (Brown and Brown, 1941); Persia (Hedayat *et al.*, 1970); India (Anderson, 1962; Aurora, Ramalingaswami and Gaitonde, 1964); Thailand (Gershoff, Prien and Chandrapanond, 1963; Halstead and Volyasevi, 1967); Laos (Westermeyer, 1971); Indonesia (Maruna, 1959; Tan, 1964); to China (Thomson, 1921) and Japan (Inada *et al.*, 1958).

The absence of bladder stones amongst poor children in the maize-eating areas of Africa may be significant (Vermooten, 1941). Processing does not lower the phosphate content of this cereal. Lonsdale, Sutor and Wooley (1968) have shown that the major constituent of endemic bladder stone is ammonium acid urate, though in certain areas of Thailand where a diet high in oxalate content is consumed, bladder stones contain appreciable amounts of calcium oxalate (Suvachittanont, Meksongsee and Dhanamitta, 1973).

In infected stones, the presence of calcium carbonate and magnesium ammonium phosphate has been detected, but not in those where the urine has been reported to be sterile. The remarkable feature of the stones we have analysed has been their very high content of ammonium acid urate with minimal quantities of inorganic material. Oxalate has been usually absent from the analyses.

Urine analysis shows that the poor children have a high acid load to excrete through the urinary tract. The urine of all children is usually moderately acid, but the rice diet consumed (Sherman and Gettler, 1912) and attacks of diarrhoea both add to urinary acidity.

We have shown that the buffering of this acid load by phosphate buffer is inadequate (probably because of a poor phosphate content of the diet), and high levels of ammonium ion are produced by the kidneys. Urinary infection does not account for this excess ammonia as only about half the children with bladder stones have infected urinary tracts, and coliform organisms, rather than *B. proteus*, are often present. Ammonia/creatinine ratios are higher in the patients with non-infected urine than normal controls. It is possible that increased production of glutamine in the liver is a necessary precursor for the renal production of ammonia (Pitts, 1973). An excess of glutamine fed into the purine production cycle might be expected to result in increased formation and excretion of urate even though glutamine is not usually regarded as a rate-regulating factor in the production of uric acid.

In Thailand, where oxalates are found to be components of children's vesical calculi due to a diet high in oxalate, a low urinary phosphate might be expected to encourage crystal growth. There is evidence that phosphate supplements to the diet of children in this area reduce the incidence of bladder stones (Chulkaratana, Van Reen and Valyasevi, 1972).

Summary

Bladder stone is a relatively common disease of childhood in West Sumatra with an incidence of 8·3/100,000 population per year.

We have studied 87 cases with a peak age of onset of 2-4 years and a male/female ratio of 12:1. The majority of these are from poor families with a diet low in protein and phosphate. Diarrhoea is common. The composition of the stones is primarily ammonium acid urate.

Patients with sterile urine have shown significantly higher levels of urinary ammonia than controls, and only approximately 50% of patients' urine were infected. This is consistent with excretion of a high acid load, due both to an acidogenic rice diet and diarrhoea, combined with a low level of phosphate.

This condition was once endemic in Europe but is now confined to a belt of countries from the Balkans through Asia.

The authors would like to acknowledge financial assistance received from the Royal Perth Hospital, Research Foundation and University of Western Australia, work done by the laboratories of the Royal Perth Hospital, Research Centre, and the co-operation of the Dean of the Faculty of Medicine, University of Andales, Dr Soemarto and Dr Mispah of Bukittingi.

References

ANDERSON, D. A. (1962). The nutritional significance of primary bladder stones. *British Journal of Urology*, **34**, 160-177.

AURORA, A. L., RAMALINGASWAMI, V. and GAITONDE, P. D. (1964). Bladder stone disease in children in the Delhi area. *Journal of Urology*, **91**, 347-353.

BROWN, R. K. and BROWN, E. C. (1941). Urinary stones: a study of their etiology in small children in Syria. *Surgery*, **9**, 415-424.

CHESELDEN, W. (1723). *A Treatise on the High Operation for the Stone*. London: Osborn.

CHULKARATANA, S., VAN REEN, R. and VALYASEVI, A. (1972). Studies on bladder stone disease in Thailand. XV. Factors affecting the solubility of calcium oxalate. *Investigative Urology*, **9**, 246-250.

CIVIALE, J. (1838). *Traité de l'Affection Calculeuse*. Paris: Crochard.

CROSSE, J. G. (1835). *A Treatise on the Formation, Constituents and Extraction of the Calculus*. London: Churchill.

ECKSTEIN, H. B. (1961). Endemic urinary lithiasis in Turkish children. *Archives of Disease in Childhood*, **36**, 137-145.

GERSHOFF, S. N., PRIEN, E. L. and CHANDRAPANOND, A. (1963). Urinary stones in Thailand. *Journal of Urology*, **90**, 285-288.

HALSTEAD, S. B. and VALYASEVI, A. (1967). Studies of bladder stone disease in Thailand. 3. Epidemiologic studies in Ubol province. *American Journal of Clinical Nutrition*, **20**, 1329-1339.

HEDAYAT, S. H., AMIRSHAHY, P., MOATAMED, K. and PEZESHKAN, M. (1970). Urinary lithiasis in Iran. A retrospective study based on 2,114 operations. *Tropical and Geographic Medicine*, **22**, 416-422.

INADA, T., MIYAZAKI, S., OMORI, T., NIHIR, H. and HINO, T. (1958). Statistical study on urolithiasis in Japan. *Urologia Internationalis*, **7**, 150-165.

JOLY, J. S. (1929). *Stone and Calculus Disease of the Urinary Organs*. London: Heinemann.

LETT, H. (1936). On urinary calculus, with special reference to stone in the bladder. *British Journal of Urology*, **8**, 205-232.

LOUTFI, A., ABDEL HAMID, G., FRANCIS, M. and ABDEL SALAM, I. (1972). Study of urinary tract calculi in Egyptian children. *Journal of the Egyptian Medical Association*, **55**, 805-812.

LEVY, D. and FALK, W. (1957). Urinary calculus disease among Israeli immigrant and Arab children. *Journal of Pediatrics*, **51**, 404-412.

LONSDALE, K., SUTOR, D. J. and WOOLEY, S. (1968). Compositin of urinary calculi by X-ray diffraction. Collected data from various localities. 1. Norwich and district. *British Journal of Urology*, **40**, 33-36.

MARUNA, R. F. L. (1959). Beitrag zum Harnstein—Problem in Indonesien. *Virchows Archiv für Pathologische Anatomie und Physiologie*, **332**, 137-139.

MCCARRISON, R. (1931). The causation of stone in India. *British Medical Journal*, **1**, 1009-1015.

PITTS, R. F. (1973). Production and excretion of ammonia in relation to acid-base regulation. In *Handbook of Physiology*, Section 8, Renal Physiology. Baltimore: Williams and Wilkins, Chapter 15, pp. 455-496.

RAČIĆ, J. (1935). Calculus of the bladder in Dalmatia. *Urologic and Cutaneous Review*, **39**, 158-163.

SHERMAN, H. C. and GETTLER, A. O. (1912). The balance of acid-forming and base-forming elements in foods, and its relation to ammonia metabolism. *Journal of Biological Chemistry*, **11**, 323-338.

SUVACHITTANONT, O., MEKSONGSEE, L. A. and DHANAMITTA, S. (1973). The oxalic acid content of some vegetables in Thailand, its possible relationships with bladder stone disease. *Journal of the Medical Association of Thailand*, **56**, 645-653.

TAN, R. E. (1964). Some observations on the etiology of bladder stones in Indonesia. *Acta Urologica Belgica*, **32**, 491-501.

TEOTIA, M. and SUTOR, D. J. (1971). Crystallisation of ammonium acid urate and other uric acid derivatives from urine. *British Journal of Urology*, **43**, 381-386.

THOMAS, J. M. R. (1949). Vesical calculus in Norfolk. *British Journal of Urology*, **21**, 20-23.

THOMSON, J. O. (1921). Urinary calculus at the Canton Hospital, Canton, China. *Surgery, Gynecology and Obstetrics*, **32**, 44-55.

VERMOOTEN, V. (1941). The incidence and significance of the deposition of calcium plaques in the renal papilla as observed in the Caucasian and Negro (Bantu) population in South Africa. *Journal of Urology*, **46**, 193-200.

WESTERMEYER, J. J. (1971). Urinary calculi in Laos. *Journal of American Medical Association*, **217**, 82-83.

YELLOLY, J. (1829). Remarks on the tendency to calculous diseases: with observations on the nature of urinary concretions, and an analysis of a large part of the collection belonging to the Norfolk and Norwich Hospital. *Philosophical Transactions of the Royal Society of London*, **119**, 55-81.

The Authors

Kamardi Thalut, MD, Surgeon, Padang General Hospital.
Ahmad Rizal, MD, Surgical Registrar, Padang General Hospital.
J. G. Brockis, ChM, FRCS, FRACS, Associate Professor, University of Western Australia.
R. C. Bowyer, PhD, Biochemist, Royal Perth Hospital, Western Australia.
T. A. Taylor, FRACS, Senior Surgical Registrar, Royal Perth Hospital.
Z. S. Wisniewski, MBBS, Surgical Registrar, Royal Perth Hospital.

Correspondence to: J. G. Brockis, University Department of Surgery, P.O. Box X2213, Perth, Western Australia.

British Journal of Urology (1976), **48**, 623-629 ©

Distension Therapy for the Unstable Bladder: Later Results including an Assessment of Repeat Distensions

P. D. RAMSDEN, J. C. SMITH, M. DUNN and G. M. ARDRAN

The Department of Urology and the Nuffield Institute for Medical Research, Oxford

Urgency and urge incontinence of urine remains one of the largest unsolved problems facing urologists at the present time.

An earlier publication from this centre (Dunn, Smith and Ardran, 1974), following the original work of Helmstein (1972), suggested that bladder distension therapy may be a useful technique in the management of those patients with urgency and urge incontinence demonstrated to have an unstable bladder.

The aim of this present paper is to present our current results with particular reference to the longer term results, and those following second distensions.

Selection of Patients

All patients selected for study had a history of urgency, urge incontinence or enuresis.

Urinary infection and urinary tract abnormality were excluded by a full urological examination.

Neurological abnormalities were excluded by clinical examination. 2 patients have developed progressive neurological signs since distension, with a probable diagnosis of multiple sclerosis, and have not been included.

In all patients drug therapy had failed to produce a satisfactory improvement. All were sufficiently incapacitated to undergo an untried procedure and the cystometrogram had demonstrated an unstable bladder.

Procedure

Preoperative cystourethrography and cystometry was carried out on all patients using the techniques described by Moolgaoker *et al.* (1972) and Dunn *et al.* (1974).

Prolonged bladder distension was carried out under high epidural anaesthesia. After preliminary cystoscopy a balloon catheter was introduced into the bladder.

An 18 Foley catheter with a condom securely tied was used in males and a Blandy catheter in females.

The bladder was distended to a pressure equal to the patient's systolic blood pressure (with an additional 15 cm water pressure to overcome the elasticity of the balloon) for four 30-minute periods, with decompression in between.

At the end of the procedure the balloon was removed and the bladder drained overnight with a Foley catheter.

The patient was discharged home on the resumption of normal micturition, usually the next day.

Read at the 32nd Annual Meeting of the British Association of Urological Surgeons in London, June 1976.

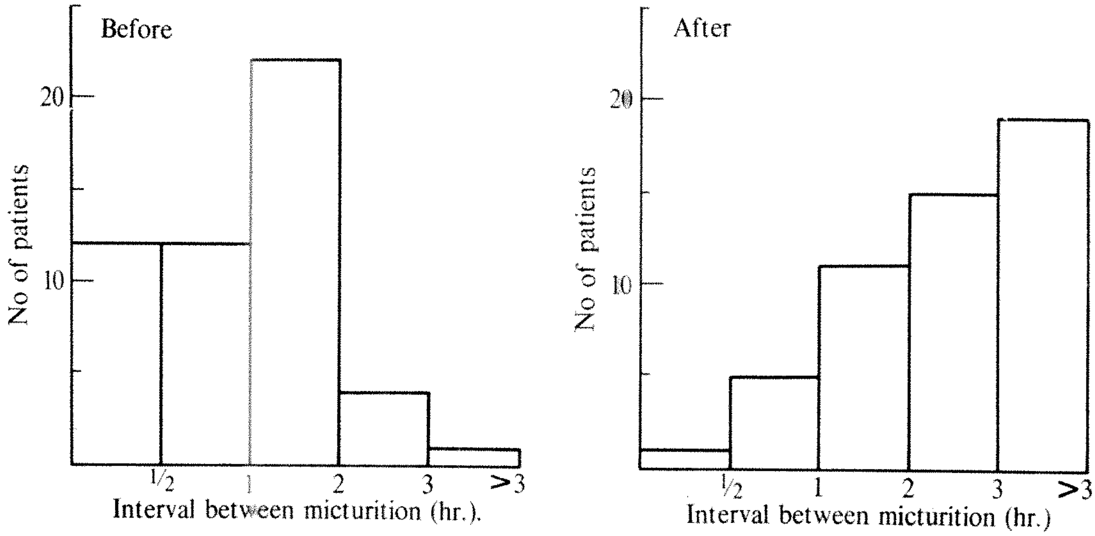


Fig. 1. Urinary frequency before and following prolonged bladder distension in 51 patients.

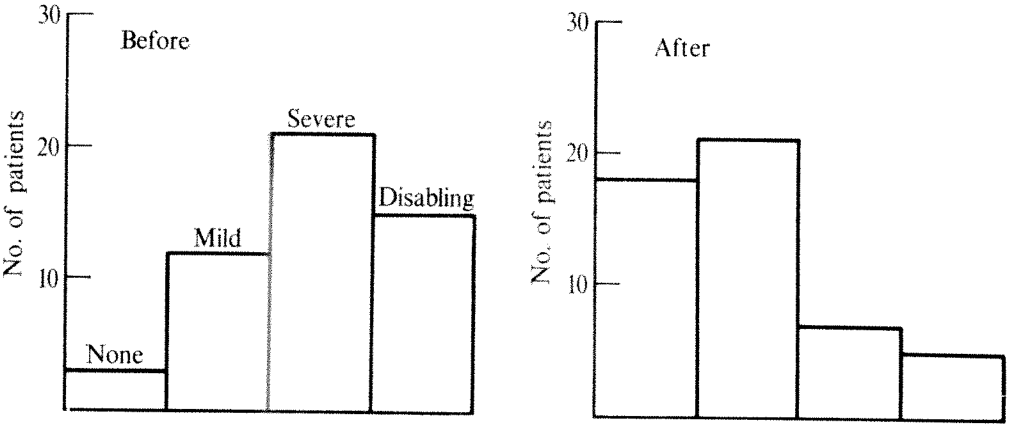


Fig. 2. Urge incontinence before and following prolonged bladder distension in 51 patients.

Results

51 patients with severe urgency, urge incontinence and enuresis have been treated by prolonged bladder distension. Symptomatic assessment has been carried out on all patients at intervals postoperatively and in 46 patients this has been combined with further pressure flow studies.

The ages of the patients ranged from 12 to 72 years with a majority in the younger age-groups. 35 were female and 16 male. Many of the patients had long histories, 15 patients having symptoms between 10 and 20 years, and 12 more than 20 years. Follow-up was from 1 month to 30 months with a mean of 13 months. The symptoms of the patients before and following prolonged bladder distension are summarised in Figures 1-4.

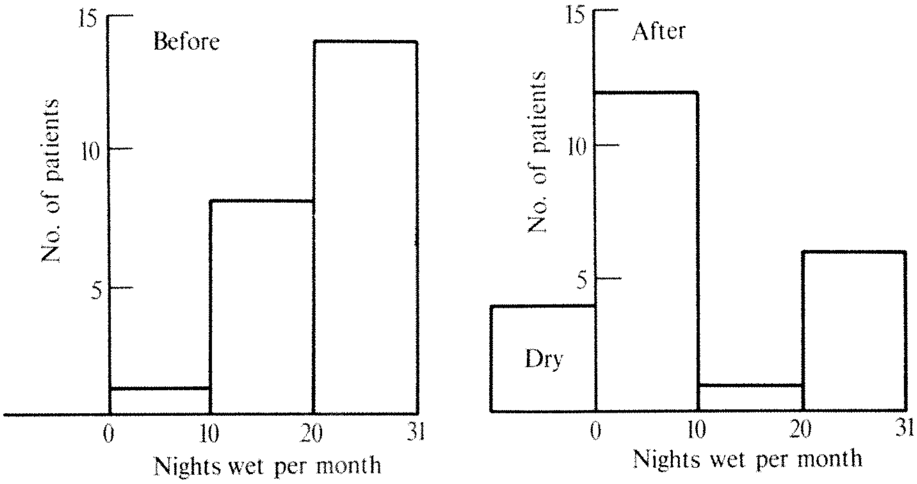


Fig. 3. Nocturnal enuresis before and following prolonged bladder distension in 23 patients.

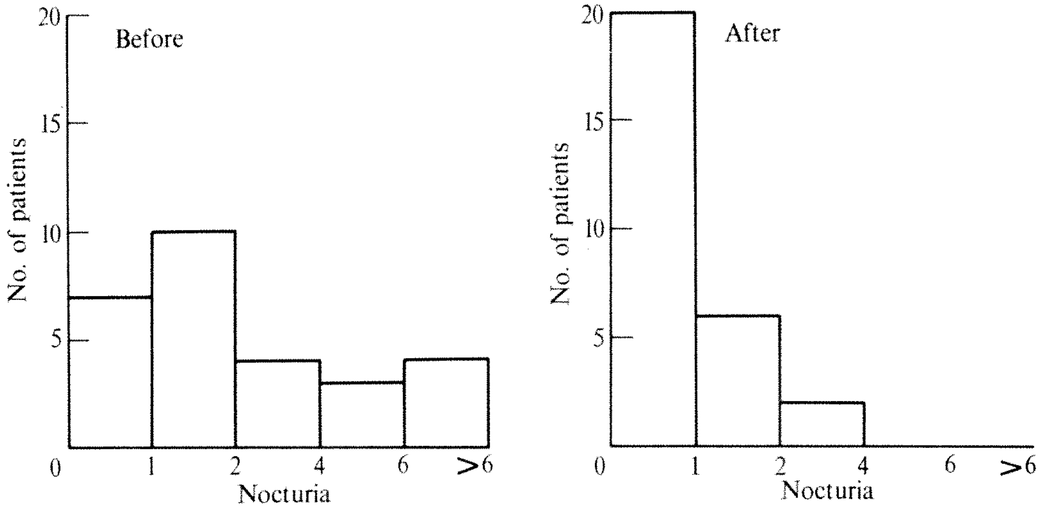


Fig. 4. Nocturia, in 28 patients with no enuresis, before and following prolonged bladder distension.

In each figure the patients have been categorised in relation to the severity of their symptoms and the overall number of patients in each group has been compared before and following prolonged bladder distension.

For the majority of patients, urge incontinence (Fig. 2) was their most distressing symptom. For pre- and postoperative comparison the patients were classified into 4 groups:

None	
Mild	patients with subjective urgency and perhaps very occasional urge incontinence;
Severe	patients with regular episodes of urge incontinence;
Disabling	patients who were constantly wet or had urge incontinence prior to every micturition; almost all of these patients had to wear protective clothing or an appliance.

Table I

Overall Result after Prolonged Distension showing the Distribution of Patients with Stable Bladders

	Overall result	Post-op cystometry
Symptom free	16	12 stable
		2 unstable
Improved	25	8 stable
		15 unstable
Same	10	1 stable
		8 unstable
Worse	0	—
	51	46

Table II

Repeat Distension. Results in 13 Patients with more than one Distension. Mean Follow-up 9 months (range 1-24 months)

Symptom free	2
Improved	6
Same	5
	13

At recent assessment, 16 patients were symptom free, 25 had a substantial improvement and 10 were symptomatically unchanged following prolonged bladder distension.

Postoperative cystometry was carried out at intervals in 46 patients. Preoperatively all patients were demonstrated to have an unstable bladder with either spontaneous contractions on filling or induced contractions at capacity. Recent postoperative studies show that 21 patients now have stable bladders (Table I). Of 43 patients who leaked urine during cystometry prior to distension, 23 patients had no leakage postoperatively.

The change in bladder capacity, measured at cystometry before and following prolonged bladder distension is shown in Figure 5. The increase in bladder capacity observed is highly significant ($P < 0{\cdot}0001$).

Maximum urinary flow rates have been compared before and following prolonged bladder distension. Many patients preoperatively had reduced bladder capacities, and because of the unreliability of flow rate estimations at small volumes (Smith, 1968), only 18 patients whose voiding volumes were greater than 200 ml before and following distension have been included.

The mean maximum urinary flow rates on these patients before and following distension were 27·7 ml/sec and 27·5 ml/sec respectively (paired sample t test, $t = -0{\cdot}08$ on 17 degrees of freedom, *i.e.* no significant difference).

Second Distensions

13 patients have had second distensions. 11 were improved after their first distension (from 1 month to 8 months—mean 3·7 months) and further distensions were carried out either because of a relapse of the patient's symptoms or because the patient, encouraged by the improvement so far achieved, requested a further distension. 2 had no response to the initial distension.

On each occasion the period of distension was increased usually to 4 periods of 1 hour, with decompression in between. The results following repeat distensions are shown in Table II.

Complications

Extra-peritoneal bladder ruptures, confirmed by cystography were sustained by 2 patients (Fig. 6). Both patients were managed conservatively with a 10-day period of catheter drainage. Further cystograms showed no leakage and the catheters were removed uneventfully. Both patients have had a good symptomatic result.

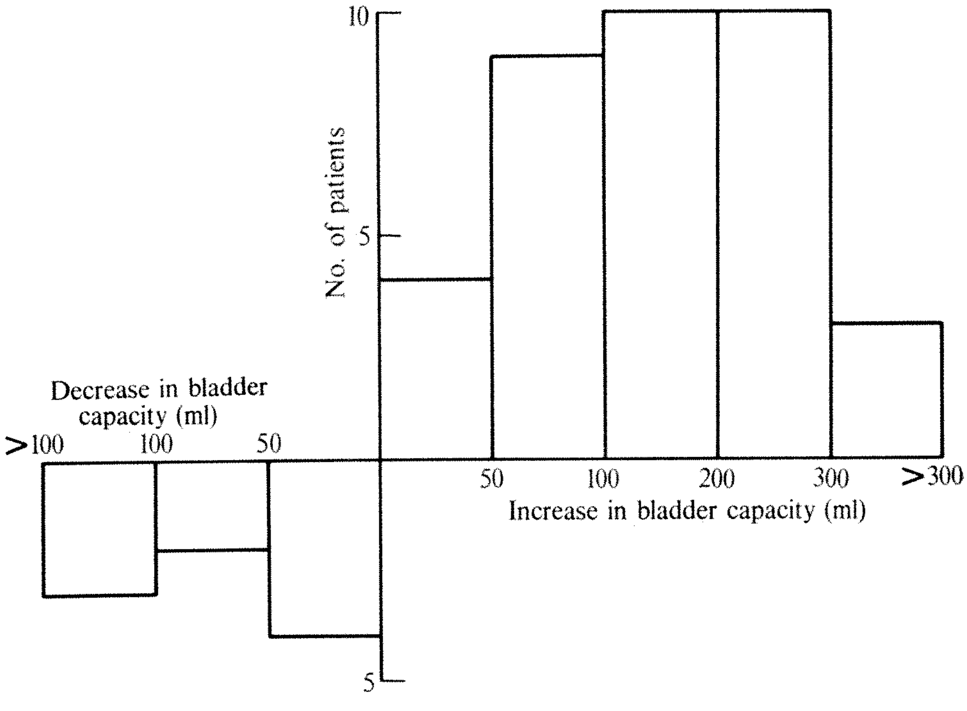
3 other patients have developed acute retention of urine requiring catheterisation, in the immediate postoperative period, but normal voiding subsequently ensued.

Discussion

Our early results have been sufficiently encouraging for us to continue the same regime. The time, pressure and intermittent type of distension were originally chosen empirically as being unlikely to produce permanent damage to the bladder wall.

Recent work from this centre (Sehn, 1976), and by Gosling, Dixon and Dunn (1976), has failed to demonstrate damage to muscle nexuses or increase in deposition of intercellular collagen following distension, previously reported by Mayo *et al.* (1973).

Sehn has shown axonal degeneration on electron microscopy occurring in the bladders of rat and rabbit during the first month after 6-hour distensions. This has been followed by apparent



Mean pre-op capacity — 269.5 mls.
Mean post-op capacity— 380.9 mls.
Mean increase in capacity—111.4 mls.
($P < 0.0001$–Wilcoxon matched pair test)

Fig. 5. Change in bladder capacity recorded at cystometry following prolonged bladder distension in 46 patients.

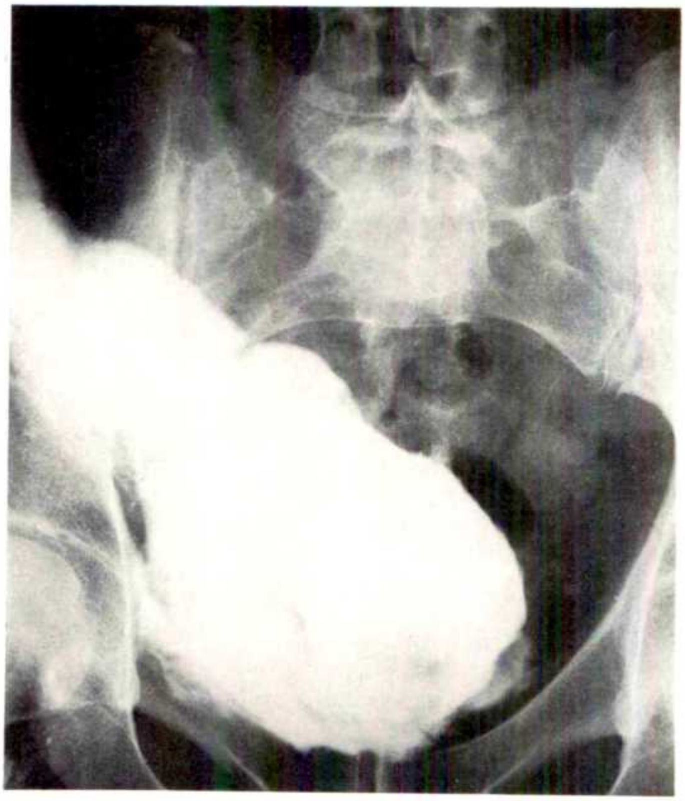


Fig. 6. Cystogram demonstrating extraperitoneal leakage of contrast from a rupture of the bladder, sustained during prolonged bladder distension.

regeneration, although it is not known whether these axons return to normal function. Similar changes were not observed after 2-hour distensions.

These findings offer some support to the hypothesis that the action of bladder distension is on the neurone terminals within the bladder wall.

The bladder appears to tolerate distension well, and persistent difficulty in voiding has not been experienced. Neither have we observed contracture of the bladder, previously reported following 6-hour distensions in patients with carcinoma of the bladder (many of whom had received other local treatment and radiotherapy)—Anderson *et al.* (1975). Patients having second distensions have shown an increase in the capacity recorded at the end of distension, when compared with that after the initial distension.

In the absence of an underlying urological or neurological abnormality the aetiology of urge incontinence of urine and the associated bladder instability remains obscure. Drug treatment may be successful in the milder cases but fails in the more severe ones. Prolonged bladder distension is a simple technique with low morbidity, and although not successful in all patients, does offer to many a marked degree of improvement in their symptoms.

Summary

51 patients with urgency and urge incontinence of urine and enuresis have been treated by prolonged bladder distension. At recent follow-up, 16 patients were symptom free, 25 substantially improved and 10 symptomatically unchanged, at a mean of 13 months after distension.

13 patients whose symptoms relapsed after a previous distension or who failed to obtain a satisfactory improvement have had a further distension for a more prolonged period. The early results in this group are not as good as for patients having first distensions, although 2 patients have become symptom free, and 6 have shown a substantial symptomatic improvement.

We wish to thank Miss Penelope Fursdon and Miss Wendy Hills for their technical assistance with the cystourethrography and cystometry. For their expert help with the epidural anaesthesia we are indebted to our anaesthetic colleagues; particularly Dr Bryce-Smith. We are grateful also to Mrs Jenny Pierce who has carried out the statistical analysis, the Department of Medical Illustration, Radcliffe Infirmary, for help with the illustrations, and to Mrs Jean Broadis for her kindness and patience in the preparation of the manuscript.

This work forms part of a Thesis to be submitted (by P. D. R.) to the University of London for the degree of Master of Surgery.

References

ANDERSON, J. D., ENGLAND, H. R., MOLLAND, E. A. and BLANDY, J. P. (1975). The effects of overstretching on the structure and function of the bladder in relation to Helmstein's distension therapy. *British Journal of Urology*, **47**, 835-840

DUNN, M., SMITH, J. C. and ARDRAN, G. M. (1974). Prolonged bladder distension as a treatment of urgency and urge incontinence of urine. *British Journal of Urology*, **46**, 645-652.

GOSLING, J. A., DIXON, J. S. and DUNN, M. (1976). The structure of the rabbit urinary bladder following experimental distension. *Investigative Urology* (in press).

HELMSTEIN, K. (1972). Treatment of bladder carcinoma by a hydrostatic pressure technique. *British Journal of Urology*, **44**, 434-450.

MAYO, M. E., LLOYD-DAVIES, R. W., SHUTTLEWORTH, K. E. D. and TIGHE, J. R. (1973). The damaged human detrusor: functional and electron microscopic changes in disease. *British Journal of Urology*, **45**, 116-125.

MOOLGAOKER, A. S., ARDRAN, G. M., SMITH, J. C. and STALLWORTHY, J. A. (1972). The diagnosis and management of urinary incontinence in the female. *Journal of Obstetrics and Gynaecology of the British Commonwealth*, **79**, 481-497.

SEHN, J. T. (1976). The ultrastructural effect of prolonged distension on the neuromuscular apparatus of the bladder. MSc Thesis, University of Oxford.

SMITH, J. C. (1968). Urethral resistance to micturition. *British Journal of Urology*, **40**, 125-156.

The Authors

P. D. Ramsden, FRCS, Research Registrar.
J. C. Smith, MS, FRCS, Consultant Urological Surgeon.
M. Dunn, MS, FRCS, Research Registrar (now Senior Registrar, Department of Urology, Bristol Royal Infirmary).
G. M. Ardran, MD, FRCP, FFR, Radiologist, Nuffield Institute for Medical Research.

Requests for reprints: Mr. J. C. Smith, Radcliffe Infirmary, Oxford.

British Journal of Urology (1976), **48**, 631-637 ©

Clinical and Experimental Studies on the Action of Prostaglandins and their Synthesis Inhibitors on Detrusor Muscle *in vitro* and *in vivo*

M. I. BULTITUDE, N. H. HILLS and K. E. D. SHUTTLEWORTH
Department of Urology, St Thomas's Hospital, London SE1

Naturally formed prostaglandins are being increasingly recognised as important pharmacological agents in many systems in the body. Interest has principally focused on reproduction, the respiratory system and the gastrointestinal tract. In a search for suitable alternatives to carbachol for the treatment of chronic retention of urine, the action of prostaglandins has been assessed experimentally on strips of bladder muscle, and clinically on a group of female patients with apparent paralysis of the detrusor.

Experiments on Isolated Strips of Mammalian Bladder

Materials and Methods

Strips of either detrusor or trigone muscle from the bladders of rabbit, rat, cat, dog, sheep, guinea-pig and human were suspended in Tyrode's solution at 37°C, bubbled with O_2 (95%):CO_2 (5%) mixture. A tension of 1g was applied. Contractions were measured isometrically and displayed on a Servoscribe 1s potentiometric recorder. Muscle strips from over 150 bladders have been examined. The effects of the following drugs have been investigated: PGE_2, $PGF_{2\alpha}$, indomethacin, meclofenamic acid, flufenamic acid, physostigmine, hemicholinium-3 and carbachol.

Results

The recording system used was found to give reproducible responses, and all preparations except the guinea-pig strip proved to be satisfactory.

Prostaglandins E_2 and $F_{2\alpha}$ were found to cause a dose-related contraction. There was, however, a relatively poor discrimination by doubling doses of prostaglandins as compared to carbachol, and a low maximum obtained (Fig. 1).

Indomethacin, a potent prostaglandin synthesis inhibitor, caused a reduction in tone and a loss of spontaneous activity over approximately 45 minutes (Fig. 2). After removal of the indomethacin there was a slow recovery. A control solution containing polyethylene glycol 200 which was used as the solvent for indomethacin, had no effect. Meclofenamic acid and flufenamic acid had a similar effect to indomethacin.

The return of tone and spontaneous activity was also restored by the addition of PGE_2 or $PGF_{2\alpha}$ (Fig. 3). Following removal of the indomethacin spontaneous recovery was again demonstrated. Bioassay of the bath fluid of rabbit detrusor strips and subsequent thin-layer chromatography indicated the presence of prostaglandin-like activity of the E series and this activity corresponded to the E_2 type. In the presence of indomethacin no prostaglandin-like activity was detectable in any experiment.

Read at the 32nd Annual Meeting of the British Association of Urological Surgeons in London, June 1976.

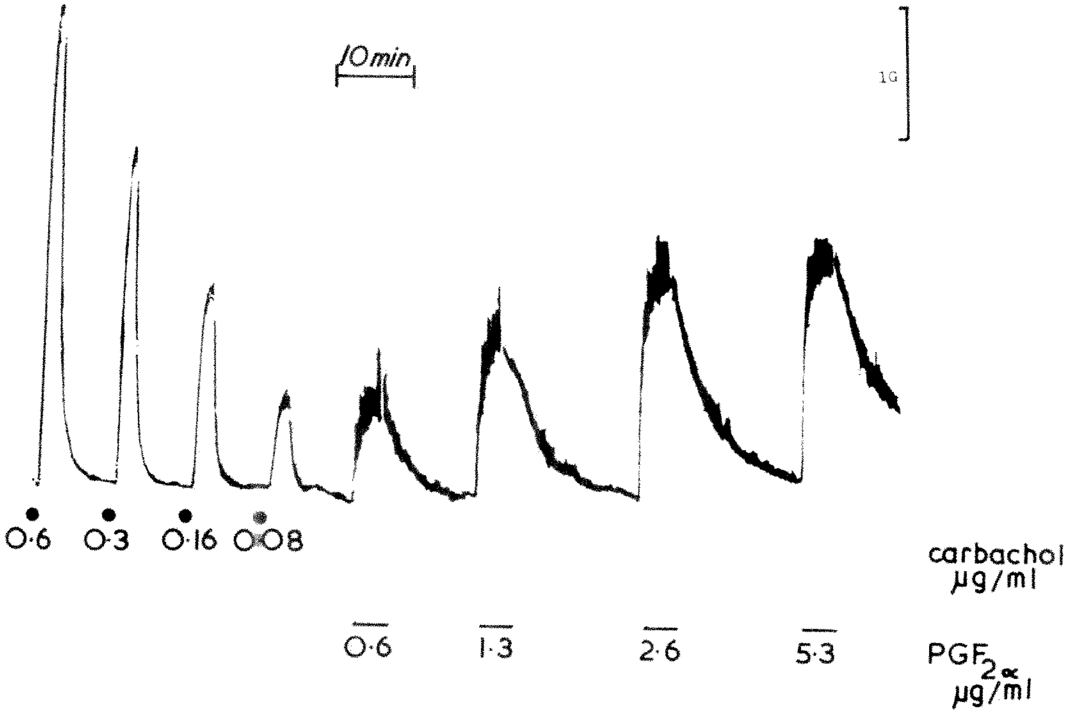


Fig. 1. Rabbit detrusor strip responses to carbachol and $PGF_{2\alpha}$.

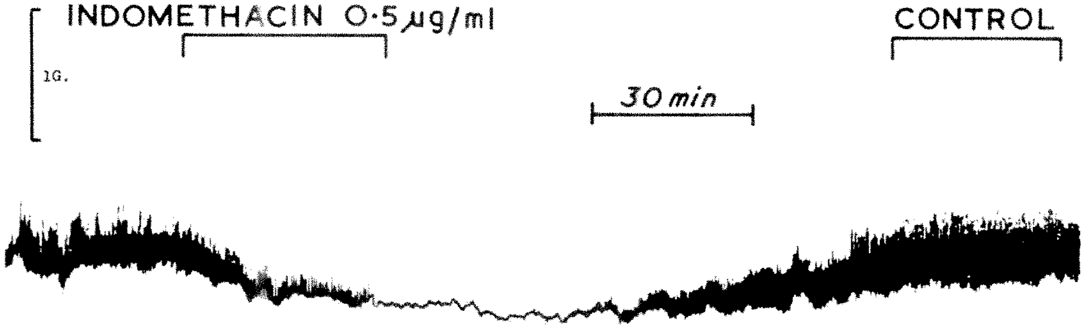


Fig. 2. Effect of indomethacin on tone and spontaneous activity of rabbit detrusor strip.

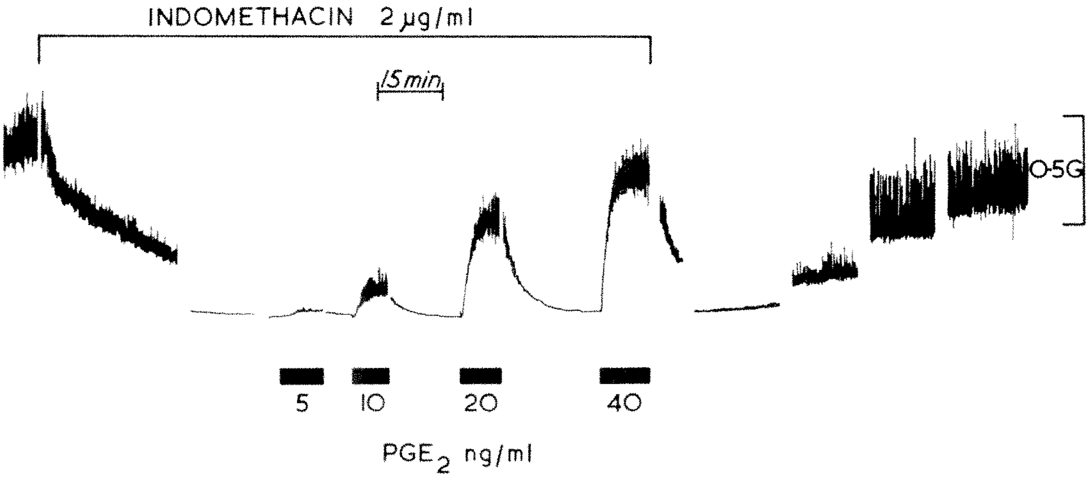


Fig. 3. Effect of indomethacin and PGE$_2$ on rabbit detrusor strip.

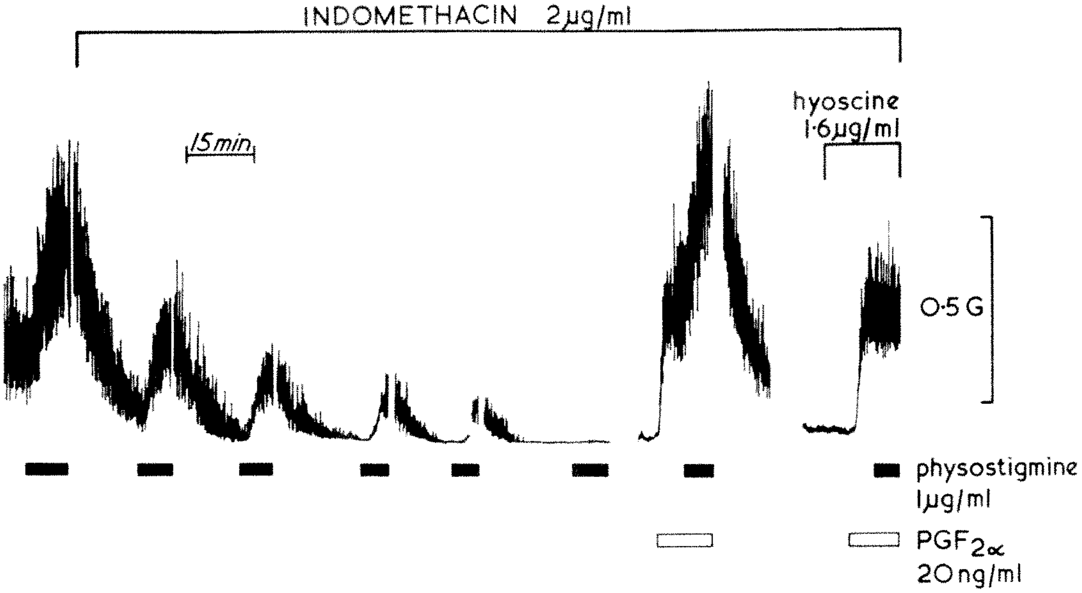


Fig. 4. Effect of indomethacin, physostigmine and PGF$_{2\alpha}$ on rabbit detrusor strip.

These results suggested strongly that the tone and spontaneous activity in the bladder muscle strips were maintained by the production of PGE$_2$.

It was further found that the tone and spontaneous activity could be increased by the addition of physostigmine to the bath fluid. An example of such an experiment is shown in Figure 4. This shows that the response to physostigmine, which in the absence of indomethacin was reproducible, became less and less. The addition of prostaglandin returned the tone and activity to its former level. This increase in tone and activity induced by physostigmine was prevented by the prior addition of hyoscine.

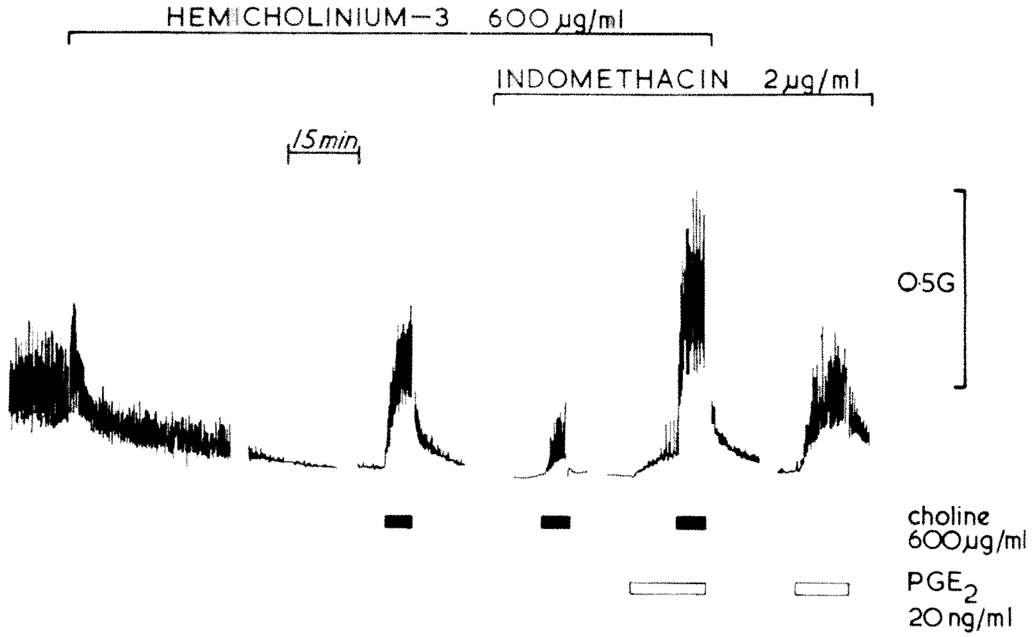


Fig. 5. Effect of indomethacin and hemicholinium – 3, alone and in combination, on the rabbit detrusor strip.

It was found that hemicholinium-3, a drug which prevents acetylcholine formation by competitively blocking the uptake of choline at nerve terminals, caused a reduction in tone and spontaneous activity. This effect was reversible by choline (Fig. 5). The addition of indomethacin resulted in no further loss of tone, but the application of choline following this resulted in a markedly smaller effect. After the addition of PGE_2 the original potency of choline was restored. Furthermore the response to PGE_2 increased when the preparation had been given time to recover from hemicholinium-3.

Patients and Methods

21 female patients presented with difficulty in micturition, and were found to be in varying degrees of chronic retention. They were shown by repeated cine cystometrogram studies to be unable to mount a detrusor contraction at any degree of bladder filling. Micturition was achieved only by abdominal straining, and the flow rate was consequently intermittent.

Cine cystometrograms were performed while the patient was seated. Bladder pressure was recorded through 1 channel of a double lumen 12F gauge urethral catheter, the other being used to fill the bladder with 35% Diodone solution at a constant rate of 50 ml/minute. Abdominal pressure was measured with a small plastic water-filled balloon in the rectum, and the flow rate during micturition by means of a Van Garrelt's flow meter. Infusion into the bladder was stopped when the patient expressed a desire to pass water. The patient was then asked to micturate; if difficulty was experienced the bladder was filled further, and the patient asked to micturate at any time. The study was repeated immediately after micturition, and performed again on another occasion. The patients were asked to confirm that the pattern of micturition exhibited under these test conditions conformed with their usual behaviour.

On the second occasion, after confirming the previous findings 0·5 mg of prostaglandin E_2 were diluted in 40 ml of sterile water and instilled into the empty bladder through a urethral catheter, which was then clamped, and the patient rested lying down for 30 minutes. At the end of this time a further cine cystometrogram was performed. No attempt was made to remove the prostaglandin solution from the bladder, but if the patient could not void at the end of the test the bladder was emptied through the catheter.

All these patients had a full clinical assessment and except as indicated did not suffer from overt neurological disorders. They were all fully apprised of the nature of the trial, to which they gave their consent, and for which they were cared for as hospital in-patients.

Results

14 of the 21 patients responded to the prostaglandins (Table I). In these a cine cystometrogram performed 30 minutes after instillation of E_2 resulted in a feeling of urgency at a much smaller volume than had previously produced a desire to micturate. This was followed by a voluntary sustained detrusor contraction with voiding. The bladder was emptied to a far greater degree than before. The achievement of voluntary micturition allowed cystograms and pressure/flow

Table I

	Before prostaglandins				After prostaglandins			
	Micturating volume (ml)	Vesical pressure (mm/Hg)	Flow rate (ml/sec)	Residual urine (ml)	Micturating volume (ml)	Vesical pressure (mm/Hg)	Flow rate (ml/sec)	Residual urine (ml)
1	1,200	0	Intermittent	1,000	400	15	24	0
2	350	0	Intermittent	200	250	25	6	100
3	850	0	Intermittent	700	350	40	16	50
4	1,000	0	Intermittent	1,000	400	20	15	200
5	1,000	0	Intermittent	800	600	20	16	100
6	1,100	0	Intermittent	700	400	25	28	50
7	1,400	0	Intermittent	800	150	20	25	0
8	400	0	Intermittent	300	200	15	16	0
9	800	0	Intermittent	800	300	22	30	0
10	600	0	Intermittent	600	150	20	16	50
11	1,200	0	Intermittent	1,200	400	22	16	50
12	800	0	Intermittent	800	350	20	15	0
13	600	0	Intermittent	300	250	24	16	50
14	500	0	Intermittent	500	350	20	18	0

Table II

	Before prostaglandins				
	Micturating volume (ml)	Vesical pressure (mm/Hg)	Flow rate (ml/sec)	Residual urine (ml)	Related pathology
1	250	0	Intermittent	200	No neurological lesion
2	300	0	Intermittent	200	No neurological lesion
3	600	0	Intermittent	200	No neurological lesion
4	800	0	Intermittent	200	Traumatic paraplegia
5	1,000	0	Intermittent	200	Abdominoperineal resection
6	600	0	Intermittent	250	Abdominoperineal resection
7	900	0	Intermittent	900	Epidural and retention: Childbirth

studies to exclude any evidence of outflow tract obstruction. Further observations on these patients showed their ability to contract the detrusor was apparently sustained, in that subjectively micturition was thereafter found to be easier and objectively the residual urine was reduced. In 5, further cystometrograms were performed which showed that detrusor contractions were indeed being maintained. Follow-up has now continued for up to 2 years, and there has been a slow return of symptoms in 3 patients 3 months after prostaglandin administration, and these have been given further instillation of prostaglandins with equally successful results.

In 7 patients no significant alteration in the cine cystometrogram was produced (Table II). In 3 of these the chronic retention was of unknown aetiology, but in the remainder neurological damage could clearly be implicated.

Discussion

It has been demonstrated that interference with the synthesis of prostaglandins in muscle strips results in a loss of tone and activity. That this activity can be restored by the removal of the synthesis inhibition or by the addition of exogenous prostaglandins suggests strongly that it is related to endogenous prostaglandin production.

The experiments using hemicholinium-3 and indomethacin demonstrated that their effects were similar, and that once the maximum effect of 1 had been achieved, no further changes were induced by addition of the other. The effects of indomethacin were reversible by means of prostaglandins and those of hemicholinium-3 by choline. In the presence of both indomethacin and hemicholinium-3, the effects of both choline and exogenous prostaglandins were reduced. This suggests that the presence of both acetylcholine and prostaglandins are necessary for the maintenance of normal tone and activity in the strips.

The intravesical route for the administration of prostaglandins in the clinical trial was chosen on the grounds of maximum safety from any side-effects of the drug. Their absorption through vaginal mucosa has been shown experimentally (Sandberg *et al.*, 1967) and it would seem likely that the bladder mucosa was penetrated in a similar fashion. The desire to micturate in response to bladder filling after administration of PGE_2 appeared at a much smaller volume than previously and it was interesting to observe that repeated cystometrograms now produced sensation amounting to urgency at this same volume. The surprising long-term effect raises the question of whether PGE_2 can indeed act over a prolonged period or whether the patients have in some way "re-learnt" the triggering mechanism for detrusor contraction. However, many of the patients had received repeated doses of carbachol with temporary relief but had not achieved lasting reflex control. The enhancement of the contractile response of uterine muscle strips to various smooth muscle stimulators by addition of PGE_2 which persisted after washing out of the prostaglandin has been described (Hall and Pickles, 1963; Clegg, Hall and Pickles, 1966) but there have been no other reports of long-term effects of prostaglandin administration.

The role of prostaglandins in bladder physiology is only partly explained by these studies. The bladder strip experiments have shown prostaglandins to be naturally produced by, and to act by increasing tone and contractility of the detrusor. Further, the use of blocking agents suggests that there is a link between the action of prostaglandins and of acetylcholine on bladder muscle, though whether this is by enhancement at the cholinergic receptor site or by a "positive feed-back" mechanism in the natural production of these agents is unexplained. It is perhaps interesting to observe that no significant changes were produced by prostaglandins in those patients with overt neurological lesions, since the latter may lead to a defect in production of acetylcholine. In 14 of the patients whose chronic retention was of unknown aetiology administration of prostaglandins was not only of diagnostic use in that with the return of detrusor contraction cine cystometrogram studies now excluded significant outflow tract obstruction, but also therapeutic in its unexpected long-term effect.

Summary

Experiments on muscle strips have shown that prostaglandin is naturally produced by the detrusor, and acts to increase the tone and spontaneous activity.

An intimate relation between acetylcholine and prostaglandin has been demonstrated.

Therapeutic application of prostaglandins has been successful in the treatment of chronic retention in women.

Upjohn Limited kindly supplied the prostaglandin E_2. This work was supported by a grant from the Endowment Fund of St Thomas's Hospital, and the muscle strip experiments were carried out in the Department of Pharmacology.

References

CLEGG, P. C., HALL, W. J. and PICKLES, V. R. (1966). The action of ketonic prostaglandins on the guinea-pig myometrium. *Journal of Physiology*, **183**, 123-144.

HALL, W. J. and PICKLES, V. R. (1963). The dual action of menstrual stimulant A2 (prostaglandin E_2). *Journal of Physiology*, **169**, 90P-91P.

SANDBERG, F., INGELMAN-SUNDBERG, A., JOELSSON, I. and RYDEN, G. (1967). Preliminary investigation on the absorption of prostaglandin E_1 from the human vagina. *Proceedings of the 2nd Nobel Symposium*. Stockholm: Almqvist and Wiksell, p. 91.

The Authors

M. I. Bultitude, FRCS, Research Senior Registrar.
N. H. Hills, FRCS, Senior Surgical Registrar.
K. E. D. Shuttleworth, MS, FRCS, Consultant Urologist.

British Journal of Urology (1976), **48**, 639-642 ©

Anti-reflux Surgery in the Congenital Neuropathic Bladder

J. H. JOHNSTON, S. R. SHAPIRO and G. G. THOMAS
Alder Hey Children's Hospital, Liverpool

Vesico-ureteric reflux is a common development in children with congenital neuropathy. When reflux occurs from a high pressure bladder and especially when, as is often the case, it is associated with infection, it is a highly dangerous complication which can rapidly cause severe hydroureteronephrosis and irreversible renal damage. It was formerly our opinion that the surgical cure of reflux should not be attempted in the neuropathic bladder and that its occurrence was an indication for urinary diversion (Johnston, 1968). However, since the late results of ileal conduit diversion have been disappointing as regards preservation of kidney function, in recent years we have adopted a more conservative attitude to the problem. Aiming at avoiding a diversion, we have been concerned in most cases, and especially with ambulant children, with lessening the urethral resistance in order to facilitate bladder emptying. Complete emptying improves upper tract drainage and, in the older child, promotes urinary continence (Johnston and Farkas, 1975). Accordingly, we have revised our views concerning the management of reflux in the congenital neuropathic bladder and the present article records our experience of ureteric re-implantation directed towards its cure.

Patients

Re-implantation was performed with 42 refluxing ureters in 28 children ranging in age from 1 year 3 months to 14 years. 20 patients had myelodysplasia associated with spina bifida or sacral anomaly. 7 had occult bladder neuropathy. 1 child showed evidence of neurological impairment following the difficult removal of a congenital intra-pelvic sacro-coccygeal teratoma. The operation was performed unilaterally in 14 patients and bilaterally in 14; in 12 of the latter both ureters were re-implanted at the same operation; in 2, separate operations were performed because of the development of contralateral reflux following a unilateral re-implantation. 30 of the refluxing ureters were associated with various degrees of hydroureteronephrosis on intravenous urography; in many of them the dilatation of the calyces was more severe than that of the ureter. 12 ureters were of more or less normal calibre although often thick-walled; in none of these cases was there significant caliectasis. The duration of follow-up after surgery has ranged from 4 months, in cases were the operation was considered unsuccessful, to 8 years.

Technique

The basic operative procedure used in all cases was the technique described by Politano and Leadbetter (1958) for transvesical ureteric re-implantation. In some instances, because of adhesive periureteritis, it was necessary to expose and dissect the ureter in the pelvis. In several, because of severe bladder sacculation, it was not possible to fashion a submucous tunnel for the ureter

Read at the 32nd Annual Meeting of the British Association of Urological Surgeons in London, June 1976.

and in these the ureter was laid against the bladder musculature in a gutter formed by incising the mucosa between the old and the new ureteric hiati. 5 severely dilated ureters were shortened and then tapered over the terminal 5 or 6 cm. When the bladder was relatively small and the ureters wide, even after tapering, the ureters were re-implanted transversely above the trigone in the manner described by Cohen (1970) in order to produce a sufficiently long intravesical ureteric segment. In 18 cases surgical widening of the vesical outlet by Y-V plasty was carried out at the time of ureteric re-implantation and in 1 case the posterior margin of the bladder neck was resected. In most of these children and in all the remainder various other measures such as urethral dilatation, the administration of phenoxybenzamine and endoscopic incision of the external sphincter and the bladder outlet were employed with the object of lessening the urethral resistance and enhancing bladder emptying at a low voiding pressure.

Results

Cure of Reflux

Cystography was performed in 26 patients at least 4 months after operation. Reflux was shown to be cured in 36 of the 38 ureters re-implanted. 2 ureters in 2 patients still had reflux; both these children later had urinary diversion performed. In the 14 cases where unilateral re-implantation had been performed, contralateral reflux developed in 7.

Upper Tract Changes

With 11 of the 12 undilated ureters re-implanted the upper tracts remained unaltered on intravenous urography. In 1 girl the system was unchanged 1 year after re-implantation but later deteriorated because of inadequate management of urinary retention in the bladder.

Excluding the 2 systems with persistent reflux, 15 of 28 initially dilated systems showed postoperative lessening of dilatation, 12 remained unaltered and 1 deteriorated. 7 of the unaltered systems stabilised at a satisfactory level; 5 whilst showing no deterioration, were still severely dilated and these 3 children and the 1 with increased dilatation after surgery underwent urinary diversion.

Discussion

Since the neuropathic bladder is generally hypertrophied and sacculated and since the ureters are frequently dilated and thick-walled and sometimes abnormally adherent to the para-ureteric tissues because of infection, the operation of ureteric re-implantation is less straightforward than in primary reflux. As a result, *secundum artem* modifications in technique are often needed to construct an adequate length of compressible intravesical ureter. Nevertheless, when ureteric re-implantation was combined with methods directed to improving bladder emptying, we have found it possible to cure reflux in 36 of the 38 ureters re-implanted in the 26 patients who had postoperative cystography performed. Contralateral reflux following unilateral ureteric re-implantation occurred in 7 of 14 cases. This is a much higher incidence than the 20% found by Parrott and Woodard (1976) to occur with primary unilateral reflux and it is now our practice in neuropathic cases to perform ureteric re-implantation bilaterally as a routine even when reflux occurs only on 1 side.

The cure of reflux was effective in preserving the upper urinary tract in 11 of 12 renal units where the tract was undilated at the time of surgery. 22 of 28 hydroureteronephrotic units either improved or stabilised at a satisfactory level (Fig. 1).

In 6 patients the operation must be considered to have failed in that conservative management was abandoned and urinary diversion performed. 2 of these children had persistent reflux and postoperative upper tract deterioration on intravenous urography. 1 patient showed increased dilatation of a solitary kidney. 2 children who had had bilateral re-implantation of severely

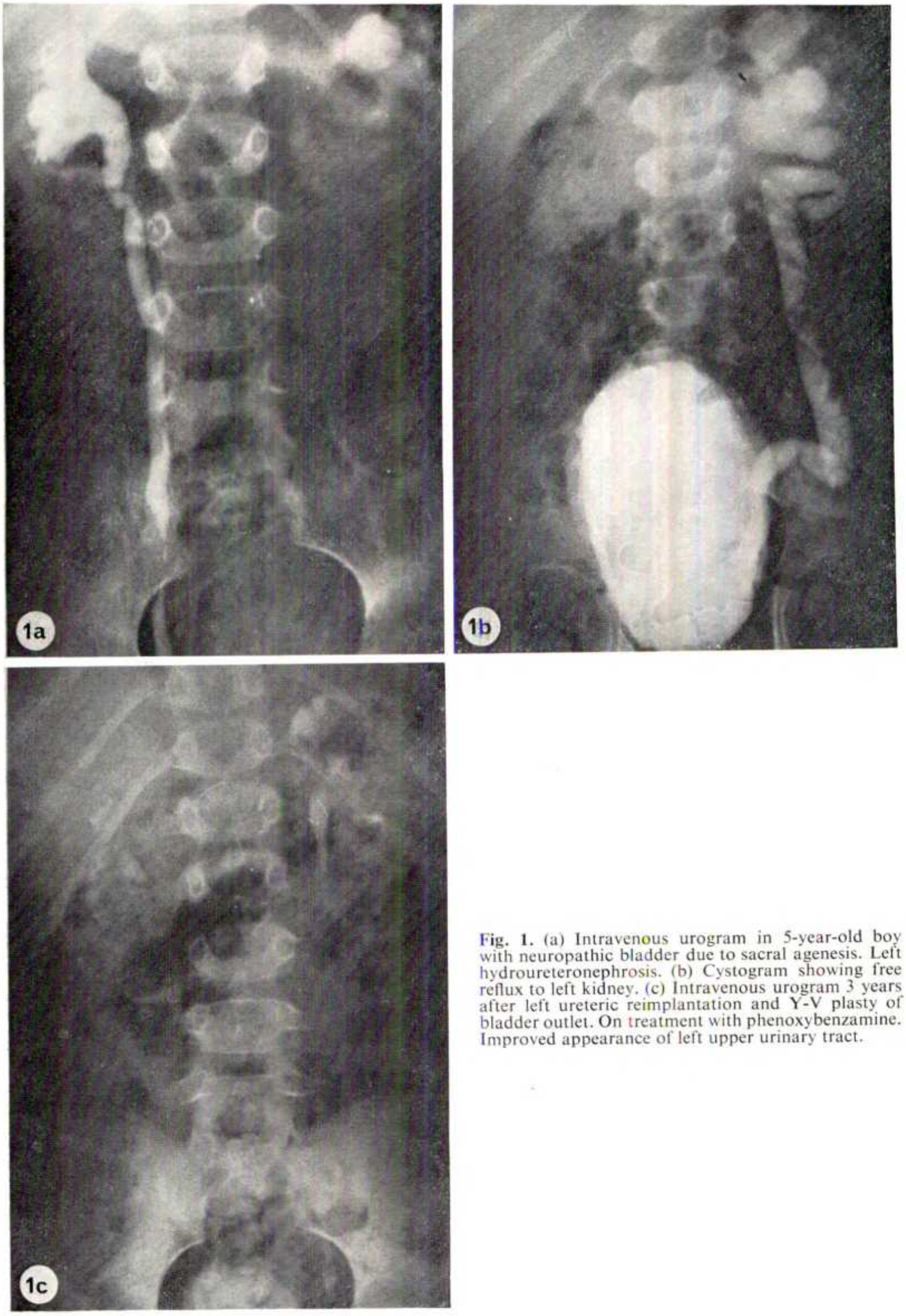


Fig. 1. (a) Intravenous urogram in 5-year-old boy with neuropathic bladder due to sacral agenesis. Left hydroureteronephrosis. (b) Cystogram showing free reflux to left kidney. (c) Intravenous urogram 3 years after left ureteric reimplantation and Y-V plasty of bladder outlet. On treatment with phenoxybenzamine. Improved appearance of left upper urinary tract.

hydroureteronephrotic systems and 1 who had a similarly dilated solitary kidney showed no pyelographic improvement 4 to 6 months after operation, and in these it was considered prudent to proceed promptly to urinary diversion. The precise reason for the operative failure in the latter 4 children was not clearly elucidated. In 3 of them a period of bladder drainage by indwelling catheter did not improve the upper tracts and it must be assumed that there was an element of obstruction at the site of re-implantation. However, the ureters were severely dilated and presumably decompensated before surgery so that only a relatively small increase in resistance at the uretero-vesical junction would be sufficient to impair ureteric drainage.

From our experience it is clear that, when combined with measures which improve bladder emptying, ureteric re-implantation in congenital neuropathic bladders can be successful in curing reflux in the majority of cases and that the existence of bladder hypertrophy and sacculation does not preclude a satisfactory result. The operation is most effective when it is performed before the development of severe upper tract changes. Since these can progress very rapidly after the onset of reflux, we believe that diagnostic cystography should be performed promptly in any child with neurological disease in whom intravenous urography shows upper tract deterioration, even if only of mild degree, or in whom the bladder is not emptying satisfactorily.

Lesser degrees of reflux can, in our experience, stop spontaneously when the urethral resistance and the bladder voiding pressure are lowered. When spontaneous cure does not occur or when the reflux is of major degree it is our contention that, if conservative management of the case is to be pursued, reflux should be cured surgically and that bilateral ureteric re-implantation is advisable even if the complication exists only on 1 side.

Summary

42 refluxing ureters were re-implanted into the bladder in 28 children with neuropathy. In each case other measures directed at enhancing bladder emptying were employed.

Reflux was cured in 36 of 38 ureters investigated after operation. The incidence of contralateral reflux following unilateral re-implantation was 50%. 1 of 12 undilated units showed late postoperative deterioration. 22 of 28 initially hydroureteronephrotic units either improved or stabilised at a satisfactory level. In 6 children urinary diversion was subsequently performed because of persistent reflux (2 cases), postoperative deterioration (1 case) or failure of severely dilated upper tracts to improve (3 cases). Since reflux from a high pressure bladder can rapidly cause severe renal damage, cystography is indicated when there is clinical or pyelographic suspicion of its existence. Operative cure is needed when reflux is of major degree or if, when of lesser severity, it does not stop spontaneously following improved bladder emptying resulting from therapeutic lessening of the urethral resistance.

References

Cohen, S. J. (1970). Personal communication.

Johnston, J. H. (1968). Vesico-ureteric reflux. In *Paediatric Urology*, ed. D. I. Williams. London: Butterworths, p. 192.

Johnston, J. H. and Farkas, A. (1975). Congenital neuropathic bladder: practicalities and possibilities of conservational management. *Urology*, **5**, 719-727.

Parrott, T. S. and Woodard, J. R. (1976). Reflux in opposite ureter after successful correction of unilateral vesicoureteral reflux. *Urology*, **7**, 276-278.

Politano, V. A. and Leadbetter, W. F. (1958). An operative technique for the correction of vesicoureteral reflux. *Journal of Urology*, **79**, 932-941.

The Authors

J. H. Johnston, FRCS, FRCSI, Consultant Urological Surgeon.

S. R. Shapiro, MD, Research Fellow in Paediatric Urology (now at Division of Urology, University of California, Davis, California).

G. G. Thomas, FRCS, FRCSE, Senior Surgical Registrar (now at Department of Paediatric Surgery and Urology, Sophia Children's Hospital, Rotterdam, Netherlands).

British Journal of Urology (1976), **48**, 643-647 ©

The Assessment of Sphincteric Activity in Patients following Trans-sphincteric Urethral Reconstruction

ROBERT D. SCHWARZ, JOHN W. FOOTE, DOUGLAS D. MOREHOUSE and KENNETH J. MACKINNON
Department of Urology, Royal Victoria Hospital and McGill University, Montreal, P.Q., Canada

The purpose of this study was to evaluate the functional integrity of the voluntary sphincter mechanism in patients following trans-sphincteric surgery for treatment of membranous and supramembranous urethral strictures. These strictures usually follow pelvic fractures with urethral disruption.

Patients

12 patients with documented membranous or supramembranous urethral strictures who had undergone trans-sphincteric reconstructive surgery were studied. These patients had been managed by the methods previously described (Morehouse and MacKinnon, 1969; Morehouse, Belitsky and MacKinnon, 1971). They were evaluated by means of urine flow rates and urethral pressure profiles. 8 of the strictures were the result of complete transection of the urethra at the apex of the prostate in association with pelvic fractures. The 4 other patients had strictures involving the bulbo-membranous urethra, and it was necessary to carry the scrotal skin flap through the external sphincter to the apex of the prostate.

The 8 cases whose strictures developed after pelvic fractures were divided into *primary cases* (those treated with initial suprapubic cystostomy only followed by delayed elective urethroplasty —3 patients) and *secondary cases* (initial therapy being either by a urethral catheter under traction or primary anastomosis—4 patients). The 8th case is case No. 3.

2 patients had undergone suprapubic prostatectomy before the development of their strictures, and both were continent after trans-sphincteric reconstruction. 2 patients had bulbo-membranous strictures and it was necessary to use a trans-sphincteric scrotal inlay to get above the stricture. 1 patient unfortunately had undergone a resection of his external sphincter, bladder neck and prostate prior to referral and was incontinent following trans-sphincteric surgery. His initial problem was pelvic fracture and ruptured membranous urethra (Case No. 3). Examples of the above cases will be presented below.

Methods

Each patient had a retrograde urethrogram to document the area of stricture. Those who had a suprapubic cystostomy and complete separation of the urethra had as well, a simultaneous cystogram (Fig. 3, A). Following urethral reconstruction there were no recurrent urethral strictures. Urine flow rates were normal except in one man who was found to have early prostatic obstruction. All of the patients had a urethral pressure profile study. Many variations of this study technique have been described (Brown and Wickham, 1969; Edwards and Malvern, 1974; Gleason *et al.*, 1974; Ghoneim *et al.*, 1975).

Read at the 32nd Annual Meeting of the British Association of Urological Surgeons in London, June 1976.

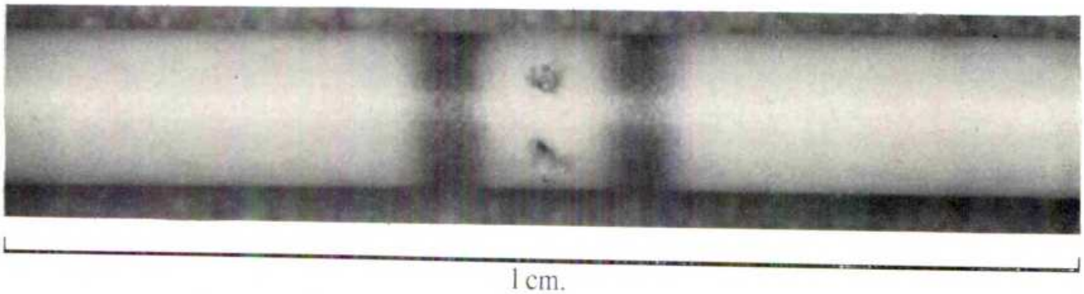


Fig. 1. The catheter used to measure the urethral pressure profile. The scale is in centimetres.

Our technique is as follows:

A Harvard pump provided a constant infusion of 0·38 cc/min through a French No. 5 catheter which had been marked in centimetres and which had 4 equally placed circumferential holes of diameter 0·5 mm (Fig. 1).

The catheter was withdrawn 1 cm each 5 seconds using a mechanised pulley system with the patient supine and relaxed. The pressure in the catheter was measured with a Statham P23AA strain gauge and recorded on a Gilson M8PM polygraph.

The resistance to flow through the lateral circumferential holes was reflected by the pressure in the catheter. The force of sphincteric action applied to the urethra round the catheter as it was withdrawn was reflected by the resistance to flow from the lateral holes.

Patients who were between stages of reconstruction presented easy access to the urethra through the perineal urethrostomy. In these patients, the catheter was re-introduced and the urethral pressure was measured under conditions of maximum voluntary sphincter contraction

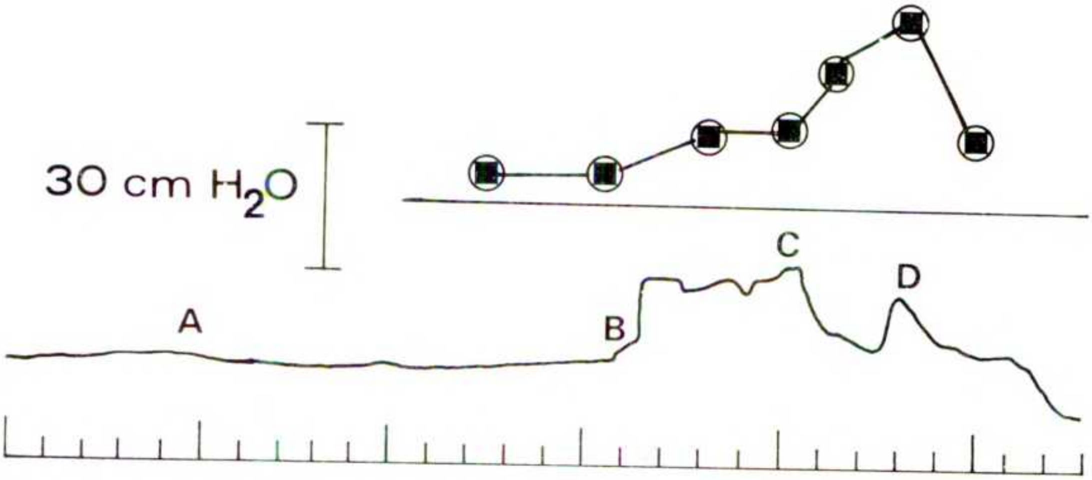


Fig. 2. Demonstrating a urethral pressure profile with the added measurement of maximum voluntary sphincteric contraction. The lowest line marks distance in centimetres from the urethrostomy. The second line shows the resting pressure profile. Point A represents intravesical pressure. The catheter is withdrawn to the bladder neck, point B, and then through the sphincteric regions, points C and D. At point C the patient has a resting sphincteric pressure of 20 cm H_2O above intravesical pressure. The catheter was then re-introduced and maximum voluntary contractions of the sphincter mechanism were measured at 7 points. The top line shows the *increase* over resting urethral pressure obtained at those points. At point D the patient can *raise* his urethral pressure 35-40 cm of H_2O above resting pressure, whereas at point C he is only able to increase by 10-15 cm H_2O.

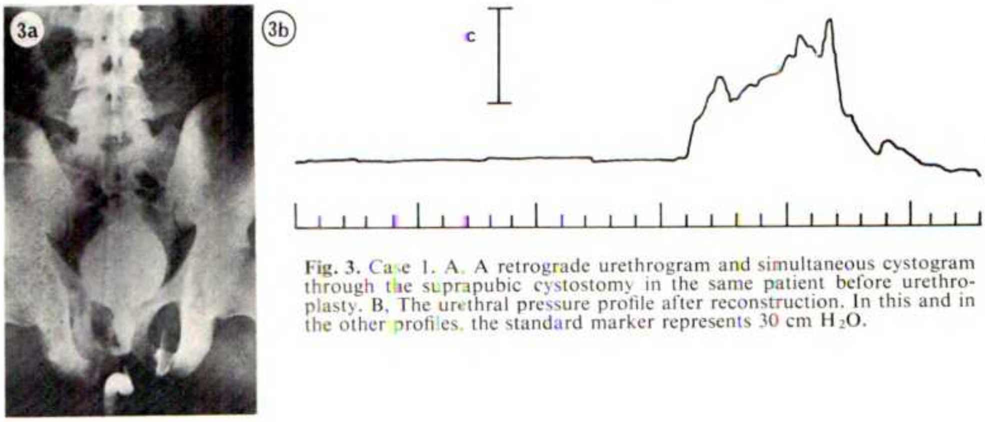


Fig. 3. Case 1. A, A retrograde urethrogram and simultaneous cystogram through the suprapubic cystostomy in the same patient before urethroplasty. B, The urethral pressure profile after reconstruction. In this and in the other profiles, the standard marker represents 30 cm H_2O.

at intervals along the urethra which had previously been identified as sphincteric. The fact that the catheter was marked allowed precise control of the position of the lateral holes. An example of such a study is presented in Figure 2.

Representative Case Histories

Case No. 1

This patient was involved in a motor vehicle accident and sustained a complete transection of the urethra at the apex of the prostate (Fig. 3, A). Initial treatment was by suprapubic cystostomy only followed by delayed elective trans-sphincteric urethral reconstruction. The patient now voids with a normal urinary flow rate and has complete continence and potency. His urethral pressure profile demonstrates a normal pattern (Fig. 3, B).

Case No. 2 (Fig. 4, A)

This man sustained a fractured pelvis with associated supramembranous urethral disruption at the time of a motor vehicle accident. He was initially treated by a catheter under traction. He underwent a 2-stage Johanson urethral reconstruction. He now voids with a normal urinary flow and is totally continent and potent. His urethral pressure profile shows normal pattern (Fig. 4, B).

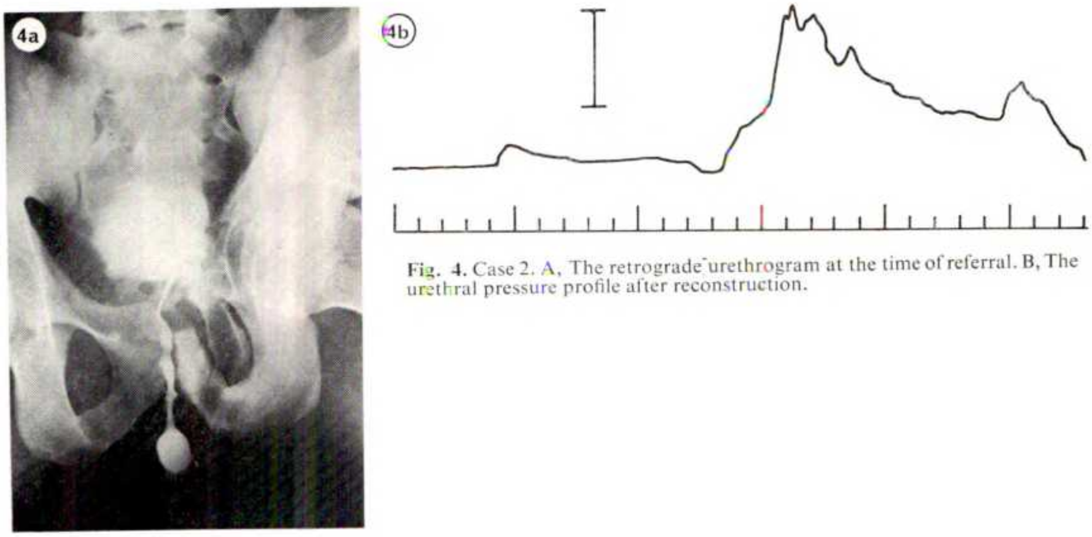
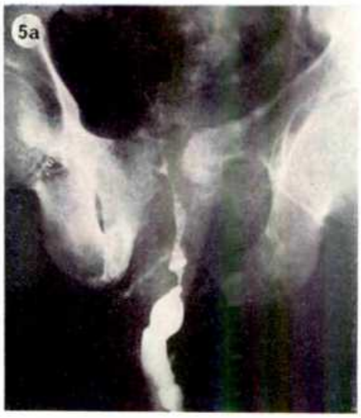


Fig. 4. Case 2. A, The retrograde urethrogram at the time of referral. B, The urethral pressure profile after reconstruction.



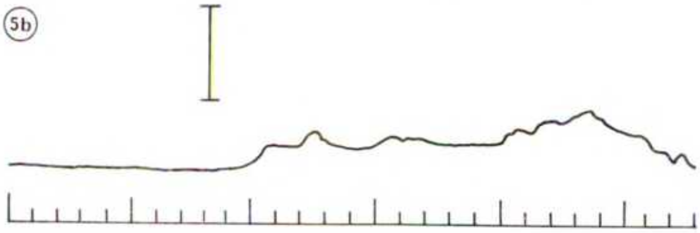


Fig. 5. Case 3. A, The retrograde urethrogram. B, The urethral pressure profile after reconstruction.

Case No. 3

This 32-year-old man ruptured the membranous urethra and fractured the bony pelvis in April 1970. He was initially treated by suprapubic cystostomy alone, but then he moved to another city where the prostate was resected transurethrally together with "fibrous tissue" in the region of the external sphincter mechanism. This resulted in an extremely dense stricture (Fig. 5, A).

Urethral reconstruction was none the less undertaken in 2 stages using the Johanson technique. He is now stricture free but is incontinent of urine and impotent.

His urethral pressure profile is distinctly abnormal in that it shows virtually no remaining sphincteric function (Fig. 5, B).

Case No. 4

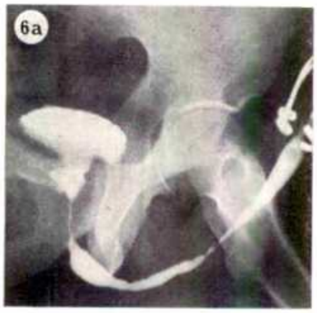
This patient underwent suprapubic prostatectomy 7 years prior to referral. He had developed strictures in the bulbo-membranous urethra as well as the penile urethra (Fig. 6, A).

A 2-stage urethral reconstruction was performed using the Johanson technique. During the first stage the scrotal flap was advanced through the external sphincter mechanism to the level of the veru montanum. The patient voids with a normal flow and is completely continent despite having a wide-open prostatic fossa and a surgically destroyed bladder neck mechanism.

The urethral pressure profile shows a sphincteric region 2½ cm in length which develops a maximum resting pressure of 35 cm H_2O above bladder pressure (Fig. 6, B). This is normal by our technique for a patient who had undergone an uncomplicated prostatectomy.

Discussion

It has been reported that the external sphincter is either irreparably damaged from the injury or from subsequent trans-sphincteric surgery. This would imply that continence in these patients is dependent on the involuntary or internal sphincter mechanism alone. Prostatectomy later



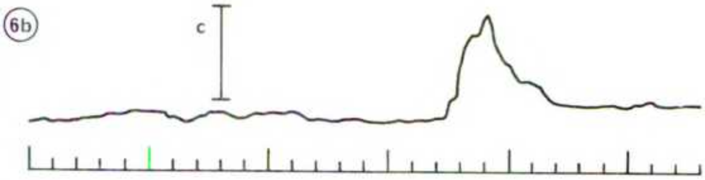


Fig. 6. Case 4. A, The retrograde urethrogram. Note the widely patent bladder neck and prostatic fossa in addition to the strictures. B, The urethral pressure profile after reconstruction.

would, by this postulate, render these patients incontinent (Turner-Warwick, 1968, 1975; Waterhouse *et al.*, 1972).

We have shown that the voluntary sphincter mechanism as measured by both resting and contracting urethral pressures can be preserved and can provide complete continence for the patient even in the absence of an involuntary sphincter mechanism. This observation has obvious implications for a group of men who may need a future prostatectomy.

Reid reviewed his experience with trans-sphincteric urethroplasties in 60 patients (Reid, 1975). Of these, 7 were patients whose strictures resulted from pelvic fracture with urethral disruption. 10 others had undergone previous prostatectomy. Of his entire group, 5 were reported incontinent, and all 5 had previous prostatectomy. It is possible that the striated sphincter had been damaged at the time of the prostatectomy *or* during the urethral reconstruction. None the less, 5 of his patients who had previous prostatectomy were continent.

There are now available several anti-incontinence devices which can be surgically implanted, but even the most enthusiastic proponent of such devices cannot claim their mechanism is as satisfactory as a normal sphincter.

Summary

12 patients who had previously undergone trans-sphincteric urethral reconstruction were studied with regard to their sphincter mechanisms. The method of study was by urethral pressure profile and urethral voluntary sphincteric pressure increment.

This study showed that patients may undergo trans-sphincteric urethral reconstruction with preservation of normal profiles and voluntary pressure increases indicating preservation of the "external" sphincter mechanism.

References

BROWN, M. and WICKHAM, J. E. A. (1969). The urethral pressure profile. *British Journal of Urology*, **14**, 211-217.

EDWARDS, L. and MALVERN, J. (1974). The urethral pressure profile: theoretical considerations and clinical application. *British Journal of Urology*, **46**, 325-336.

GHONEIM, M. A., ROTTEMBOURG, J. L., FRETIN, J. and SUSSET, J. G. (1975). Urethral pressure profile: standardization of technique and study of reproducibility. *Urology*, **5**, 632-637.

GLEASON, D. M., REILLY, R. J., BOTTACCINI, M. R. and PIERCE, M. J. (1974). The urethral continence zone and its relation to stress incontinence. *Journal of Urology*, **112**, 81-88.

MOREHOUSE, D. D. and MACKINNON, K. J. (1971). Urological injuries associated with pelvic fractures. *Journal of Trauma*, **9**, 479-496.

MOREHOUSE, D. D., BELITSKY, P. and MACKINNON, K. J. (1971). Rupture of the posterior urethra. *Transactions of the American Association of Genitourinary Surgeons*, **63**, 11-14.

REID, R. E. (1975). Turner-Warwick urethroplasty and urethral stricture: results in 60 patients. *Urology*, **6**, 711-715.

TURNER-WARWICK, R. (1968). The repair of urethral strictures in the region of the membranous urethra. *Journal of Urology*, **100**, 303-314.

TURNER-WARWICK, R. (1975). In: *Current Operative Urology*. Edited by E. D. Whitehead. Harper and Row, pp. 1053-1054.

WATERHOUSE, K., ABRAHAMS, J. I., GRUBER, H., HACKETT, R., PATIL, U. B. and PENG, B. K. (1972). The transpubic approach to the lower urinary tract. *Transactions of the American Association of Genitourinary Surgeons*, **64**, 18-22.

The Authors

Robert D. Schwarz, MD, Resident in Urology, Royal Victoria Hospital.
John W. Foote, MD, Assistant Urologist, Royal Victoria Hospital.
Douglas D. Morehouse, M.D, Associate Urologist, Royal Victoria Hospital.
Kenneth J. MacKinnon, MD, Urologist-in-Chief, Royal Victoria Hospital.

Requests for reprints: Dr Douglas D. Morehouse, Department of Urology, Royal Victoria Hospital, 687 Pine Avenue West, Montreal, P.Q., Canada.

British Journal of Urology (1976), **48**, 649-656 ©

Division of the External Urethral Sphincter in the Neuropathic Bladder: A Twenty Years' Review

J. COSBIE ROSS, N. O. K. GIBBON and G. SHAM SUNDER
Liverpool Regional Urological Centre, Liverpool, and Sefton General Hospital, Liverpool.

As in other centres interested in the neuropathic bladder, the writers followed with interest the work by Emmett (1940, 1947, 1954) and carried out a number of transurethral bladder neck resections in the early 1950s (Gibbon, Ross and Damanski, 1965). However, it was found that while some patients responded (especially those with sacral lesions), in many others the results were disappointing. At this point it became clear that in the majority of patients with suprasacral lesions the obstruction was lower than the bladder neck and was in fact at the level of the external sphincter. At that time Emmett suggested that striated muscle spasticity could be relieved not only by subarachnoid alcohol block and sacral rhizotomy but also by pudendal neurectomy. Therefore with other workers, notably Bors and Comarr (1954), a series of pudendal neurectomies were carried out with some success during the years 1952-56 (Ross and Damanski, 1953).

The earliest hint of what might be called the "low obstruction" (not due to pelvic floor spasticity), had come from Watkins of Manchester as a result of cysto-urethrographic studies, which showed that in some cauda equina lesions critical obstruction lay at the level of the urogenital diaphragm (Watkins, 1936). Later, this was followed by the observation that dilatation of the affected area of the urethra by means of a Kollman's dilator was sometimes rewarded by temporary improvement (Donovan, 1947). Donovan also suggested resecting the urogenital diaphragm but assumed that total incontinence would result. At one time it was thought that the obstruction was of mechanical origin, either a posterior angulation of the bladder and prostate (Dollfus *et al.*, 1972) or a concertina-like deformity (Vincent, 1966). However, after confirming Donovan's work the writers decided that a permanent improvement might be achieved by dividing the region of the external urethral sphincter, an operation which we first carried out in 1956 (Ross, 1956).

The operation was soon extended to include the more numerous suprasacral cases with external sphincter spasticity partly because of the high incidence (50-60 %) of impotence following pudendal neurectomy. There has been little or no complaint of impotence following sphincterotomy, though this has been reported by Thomas (1976) and Dollfus, perhaps because great care was taken to avoid encroaching on the venous sinuses of the corpus spongiosum. Although earlier results (Ross, Gibbon and Damanski, 1963, 1967) were published there was a latent period until the procedure was taken up by Currie *et al.* (1970) in the US, Walsh in the UK and O'Flynn in Eire (1972). It is now widely accepted and practised throughout the world, with a total reported experience of approximately a thousand cases.

Having reviewed the results for the first 10 years (Ross, Gibbon and Damanski, 1967) it was thought advisable to bring the findings up to date 20 years since the operation was first performed.

Rationale. Henle's century-old description of the anatomy of the circular striated external sphincter, with its inverted fan of fibres extending up in the anterior direction, still stands (Haines, 1969). This muscle is thought to

Read at the 32nd Annual Meeting of the British Association of Urological Surgeons in London, June 1976.

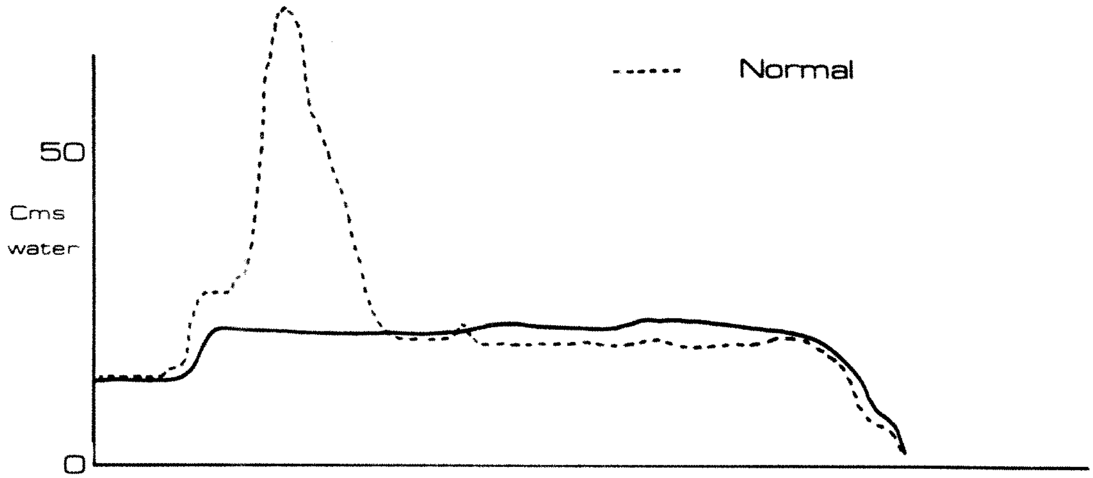


Fig. 1. Urethral pressure profile before (dotted line) and after operation in a case with a supra-sacral lesion.

play a relatively minor role in the *resting* urethral resistance which even at that level is largely due to plain muscle under sympathetic control, as has been shown by Donker, Ivanovici and Noach (1972).

The external sphincter is now known to come into action reflexly (and voluntarily), in the prevention of leakage from an overdistended bladder. It is also responsible for sudden voluntary interruption of the urinary flow and no doubt assists in the "milk-back" of the urine remaining in proximal urethra at the end of micturition. In all this the triple nerve supply must be of vital importance (Elbadawi and Schenk, 1974). However, there is no reason to suppose that the external sphincter normally plays any part in preventing leakage of urine during sudden increases of lower abdominal pressure, as under these circumstances "stress" leakage is prevented by the intra-abdominal position of the whole of the prostatic urethra and the upper part of the membranous urethra (Enhörning, 1961). This concept is supported by clinical observation *e.g.* the distal two-thirds of the female urethra may be excised during vulvectomy and in the male the membranous urethra may be subjected to a posterior skin-flap insert in a urethroplasty, with impunity. It follows, therefore, that division of the external sphincter is not followed by stress incontinence, provided the proximal urethra closes normally as it usually does in patients with a lesion above the sacral segments. In sacral lesions, however, the bladder neck tends to funnel into the flaccid pelvic floor, or the same effect may be actually encouraged by a bladder neck resection carried out in the interest of more efficient voiding. In these circumstances stress leakage is more likely.

The mechanism of the obstruction in upper motor neurone (supra-sacral) lesions has been confirmed by Diokno *et al.* (1974), who have shown how reflex detrusor action may be opposed by simultaneous sphincter contractions, or clonic spasms as well as by a varied basic tone. Hodgkinson, Ayres and Drukka (1963) considered a more accurate description would be "detrusor-sphincter dyssynergia".

The operation devised by the writers, in which two 5 mm deep incisions are made postero-laterally from the verumontanum distally, has been shown in postmortem studies to divide the striated muscle in the region (Linker and Tanagho, 1975). In the light of work carried out by colleagues and others, it would seem likely that some unstriated fibres are divided together with the external sphincter. Clinically, urethral pressure profiles provide an accurate method of confirming the completeness of the operation (Abel *et al.*, 1975) (Fig. 1).

Indications. Weight of opinion has, over the years, confirmed the writers' view that when obstruction occurs in the neuropathic bladder the site of obstruction is usually at the external sphincter level rather than at the bladder neck. Ascoli and Franch (1966) demonstrated, in cine-radiographic studies, that in 94% of paraplegic patients the bladder neck was opened widely during voiding whereas the external sphincter region failed to relax.

Similarly, Scott (1967) stated that few of his patients appeared to have obstruction at the bladder neck, whereas the external sphincter did not relax and the pelvic floor failed to descend during voiding. Scott added that the voltage potential of the sphincter in supra-sacral lesions increased rather than decreased. Again, Semans (1967) says, "After the urethra has been completely divided precisely at the junction of the urogenital diaphragm and the apex of the prostate the bladder emptied itself, proving that this was the one remaining segment of the urethra which was obstructed after transurethral resection."

This obstructive factor at the external sphincter level is, then, mainly associated with the fact that in the automatic bladder contraction of the detrusor is not accompanied by descent of the bladder base, and the urinary stream encounters resistance from the unrelaxed external sphincter.

Approximately one-quarter of the patients with traumatic paraplegia referred to the Liverpool centre required the operation and a few of these also needed a bladder neck resection. Although an image intensifier is obviously the ideal method of investigation in these patients, it has been found in the past that the ascending cysto-urethrogram is reliable and expeditious (Damanski and Keer, 1964). Recently, more reliance has been placed on simple cystometry with measurements of the urethral resistance in both the supine and sitting positions (Gibbon, 1973). With regard to timing it used to be the practice to wait 6-12 months before carrying out the operation but there is now a tendency to intervene much earlier.

Indications include:

(1) *In upper motor neurone lesions* with obstruction demonstrable at the membranous urethral level. This may involve complete retention at the end of 3 months or an appreciable residual urine, especially if associated with urinary infection. If, in addition, the bladder nech fails to open during micturition in spite of alpha-blocking agents, it may also be necessary to carry out a bladder neck resection. This set of circumstances may arise when there is inflammatory stenosis in addition to the sphincteric spasm.

(2) *In lower motor neurone lesions* with failure of funnelling of the bladder neck on voiding a bladder neck resection is obviously indicated. However, the obstruction may be at the external sphincter level from the outset or be revealed after the bladder neck resection. In either event the first line of attack should be alpha-blocking agents followed by division of the external sphincter region if necessary.

It is important to realise that these operations are not to be carried out for an arbitrary level of residual urine, whether absolute or relative to the bladder capacity. Any residual urine compatible with sterility is acceptable provided the upper urinary tract remains normal at the yearly check-ups. What is not acceptable is a residual urine which is clearly responsible for maintaining infection or is associated with vesical hypertonia, resulting in impaired ureteric emptying with hydro-ureter and hydronephrosis. Aiming at a rapid turnover at the Liverpool centre the writers tend to operate as soon as the patient is otherwise rehabilitated, often within 3 months. It is true that this policy of early intervention is opposed to that of certain other centres who are prepared to wait for a year or more (Bors and Comarr, 1971). However, the writers are firmly of the opinion that catheter drainage, whether continuous or intermittent, should be discarded at the earliest possible moment. Moreover, the follow-up figures show clearly that patients with upper urinary tract involvement, especially hydronephrosis, carry a poorer prognosis. The operation is sometimes indicated in medical paraplegia and considerable improvement may be achieved even in multiple sclerosis for a period of years (Ross, Gibbon and Damanski, 1964; Ross and Jameson, 1971; Jameson, 1974). The indications remain the same in both medical and traumatic cases.

Method

For a number of years the operation was carried out through a panendoscope, using a Colling's diathermy knife to make 2 posterolateral cuts. The upper limit of the cut is at the level of the verumontanum, an actual ridge or hump

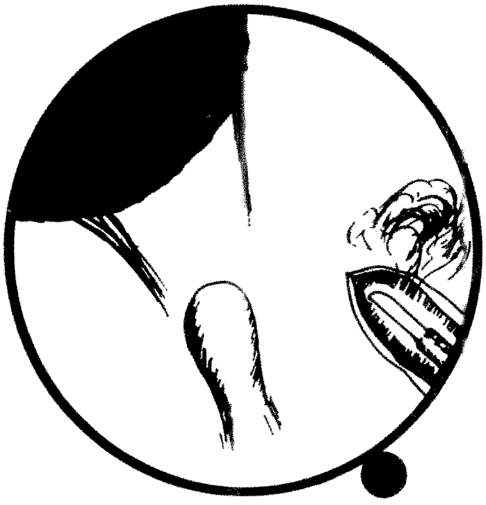


Fig. 2.

being sometimes appreciated by the extremity of the panendoscope. The minimal coagulation current which will divide the mucosa is chosen and the muscular fibres are divided a few at a time, the incision extending downwards for about 3 cm (Fig. 2). In view of Tanagho's recent work (Linker and Tanagho, 1975) it may be possible now to reduce the length of the incision to 2 cm without any loss of effect. The division is gradually deepened until the muscular wall begins to thin out. Carried out in this way the operation rarely produces more than a few small arterial bleeders and these are easily controlled with a ball electrode. Venous bleeding is rarely troublesome because the cutting current is avoided at any stage. Any residual venous bleeding ceases after the introduction of a 22 Ch catheter at the conclusion of the operation (Ross, Gibbon and Damanski, 1967). Recently, the procedure has been modified a little by using a knife electrode through a resectoscope. It is safer to do too little cutting rather than too much, especially as the operation can readily be repeated.

Patients

During the period 1956-74, 764 patients were admitted to the Liverpool Spinal Centre at Southport and, of these, 177 required division of the external sphincter (D.E.S.) or 23% (Table I).

There were almost twice as many paraplegics as tetraplegics. The operation was performed on 131 traumatic cases and 46 non-traumatic and once again the proportion of paraplegia to tetraplegia was 2 to 1.

Table I

Division of the External Sphincter

Carried out in patients with:	
Tetraplegia	59
Paraplegia	113
Cauda equina	2
Others (no precise level)	3
	177

Table II

Results of D.E.S. (1956-1974)

Elimination or considerable reduction of R.U.	157
Voiding but with a R.U. of over 200 ml	9
R.U. not known	2
Incontinent	1
Failures (on catheter)	8
	177

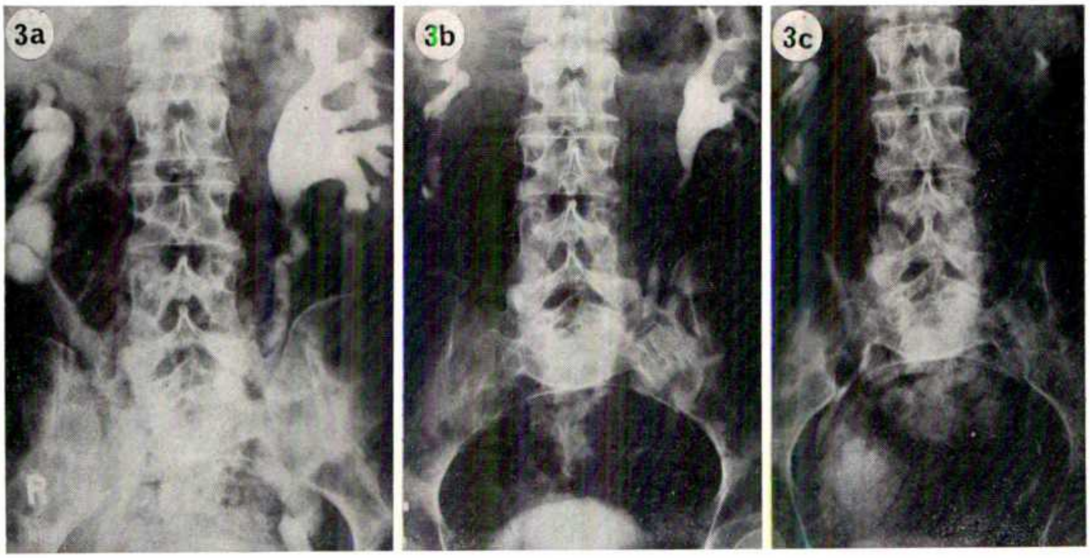


Fig. 3. A, I.V.P. before operation. B, 1 year after operation. C, 7 years after operation.

Results and Discussion

1. Residual Urine. The results show that the residual urine was either eliminated or considerably reduced in the majority of patients (Table II). Owing to the yearly follow-up it was possible to account for all but 2 cases. There were 8 failures who required an indwelling catheterisation and 1 patient was rendered incontinent. Before operation many of these patients were either unable to void or had a large residual urine.

2. Infection. The figures in Table III refer only to the later series of 112 operations *i.e.* 1966-74, and in 31 the urine remained consistently sterile. Infection was found intermittently in 24 but in the remaining 57 there was a persistent (though usually mild), infection at every follow-up.

Table III

Effect of D.E.S. on Urinary Infection (1966-74)

Urine sterile at follow-ups	31
Urine intermittently infected	24
Urine persistently infected	57
	112

Table IV

Effect of D.E.S. on the Upper Urinary Tract

Before D.E.S.	Normal I.V.P.	120
	Hydronephrosis	51
	Unknown (no I.V.P.)	3
	One kidney normal One kidney non-functioning	3
		177
After D.E.S.	Hydronephrosis disappeared	14
	Hydronephrosis improved	14
	Hydronephrosis unchanged	17
	Hydronephrosis worse	1
	Result not known	5
		51

Table V

Postoperative Mortality

Earlier series (1956-66)	2 deaths (out of 65 operations)
Later series (1966-74)	No deaths (out of 112 patients)

Table VI

Late Mortality

Earlier series (1956-66)	7 deaths (out of 65)	
Later series (1966-74)	10 deaths (out of 112)	
Cause of death (late series)	Cerebral thrombosis	1 (2 years)
	Intestinal obstruction	1 (6 years)
	Road traffic accident	1 (1 year)
	Amyloid disease and renal failure	1 (2 years)
	Renal calculus and pyelonephritis	1 (6 months)
	Unknown	5
Death occurred in unknown patients	6 years	After operation
	5 years	
	1 year	
	6 months	
	1 month	

This is disappointing but it must be pointed out that these infections were largely found in the earlier patients carried out before the narrow-bore Gibbon catheter, or the intermittent catheterisation methods were available. Persistent infection has been less a problem during the last few years.

3. Upper Urinary Tract (Table IV). Hydronephrosis is always a difficult problem in the neuropathic bladder especially as it may appear (or disappear) spontaneously without any reasonable explanation and without any evidence of obstruction. Further, as was pointed out 10 years ago, if there is any trabeculation of the bladder, or secondary changes in the ureteric orifices, elimination of obstruction further down will not necessarily result in any dramatic improvement in the X-ray appearances. However, in more than half those patients with hydronephrosis the I.V.P. showed considerable improvement or a return to normality after division of the external sphincter. Figure 3 shows the effect on the upper urinary tract 1 year and 7 years after operation.

4. Mortality (Table V). Since the present technique was adopted there has been no operative mortality in the last 167 patients. The 2 deaths in the early series were probably due to resection with the cold punch opening up venous sinuses, causing troublesome bleeding and encouraging infection by the blood stream. These mortality figures exclude those patients dying within a few weeks of admission from concomitant cerebral, thoracic or abdominal injuries, and in fact not surviving long enough to become bladder problems (Table VI).

5. Late Mortality. It was satisfactory to see that there were 58 patients still alive from the earlier series. Moreover, in the later group the actual cause of death was distributed over a wide range and occurred approximately 2½ years after the operation was performed.

Even if the 5 unknown deaths are included as being of renal origin, the mortality from renal causes is still under 6%.

6. Sexual Function (Table VII). One of the reasons for abandoning pudendal neurectomy in the fifties was that this particular procedure eliminated erections in 60% of cases whereas division of the external sphincter was thought to have no such action.

It is difficult to obtain any precise information on this particular aspect and in 51 patients, nothing about erection was recorded. Further, in 33 there were no erections from the time of the injury onwards. Although this information is scanty and unsatisfactory, it does emphasise that, unlike pudendal neurectomy, the operation does not abolish sexual function.

It has been found necessary to repeat the procedure on a number of occasions but this presents no difficulty. It is much safer to do this rather than attempt too much and get involved in bleeding from large venous sinuses of the corpus spongiosum. It is necessary sometimes to combine the operations with a bladder neck resection as is shown here (Table VIII).

Table VII

Effect of D.E.S. on Sexual Function (1966-74)

Erections recorded	28
No erections from time of injury onwards	33
No information	51
	112

Table VIII

D.E.S. Repeated or Associated with other Procedures (1966-74)

D.E.S.	42
D.E.S. repeated	13
D.E.S. preceded by B.N.R.	18
D.E.S. combined with B.N.R.	16
Multiple operations	20
D.E.S. alone or in combination with B.N.R. preceded years earlier by pudendal neurectomy	3
	112

Conclusions

When obstruction occurs in the neuropathic bladder the site is more frequently at the external sphincter level than at the bladder neck.

The obstruction can be safely and efficiently dealt with by division of the external sphincter region.

As a result of the operation residual urine and infection are eliminated or considerably reduced.

If secondary changes in the bladder and upper urinary tract are not fully established, improvement may also be expected in renal function, ureteric reflux and hydronephrosis.

Summary

It is now twenty years since the authors first performed division of the external sphincter region in the treatment of the neuropathic bladder. Although a ten year report was published in 1967, it was decided to review all the patients at the end of the twenty year period. The rationale of the operation in the upper motor neurone lesion has been confirmed by modern investigative techniques, while it appears from recent work that the success of the procedure in the lower motor neurone case is due to division of plain muscle which is subjected to excessive sympathetic stimulation.

It is the authors' firm conviction that long term catheterization, whether permanent or intermittent is a confession of failure and can be avoided in the vast majority of patients. The operation has proved of permanent benefit especially with the regard to the elimination of residual urine. Further, hydronephrosis, and renal infection and failure, are also benefited in many cases. These factors are of great importance in a condition in which late morbidity and mortality has been usually due to renal causes.

References

ABEL, B. J., ROSS, J. COSBIE, GIBBON, N. O. K. and JAMESON, R. M. (1975). Urethral pressure measurement after division of the external sphincter. *Paraplegia*, **13**, 37-41.

ASCOLI, R. and FRANCH, L. (1966). Studio radiologico del collo vesicale nei paraplegici da trauma midollare. *Urologia Internationalis*, **33**, 384-399.

Bors, E. and Comarr, A. E. (1954). Effect of pudendal nerve operations on the neurogenic bladder. *Journal of Urology*, **72**, 666–670.

Bors, E. and Comarr, A. E. (1971). *Neurological Urology*. Baltimore, University Park Press.

Currie, R. J., Bilbisi, A. A., Schiebler, J. C. and Bunts, R. C. (1970). External sphincterotomy in paraplegics. *Journal of Urology*, **103**, 64-68.

Damanski, M. and Keer, A. S. (1964). Paraplegia of non-traumatic origin and disseminated (multiple) sclerosis: urinary complications, their nature and treatment. *Acta neurologica et psychiatrica Belgica*, **64**, 495-519.

Diokno, Ananias C., Koff, S. A. and Bender, L. F. (1974). Peri urethral striated muscle activity in neurogenic bladder dysfunction. *Journal of Urology*, **112**, 743-749.

Dollfus, P., Jurascheck, F., Jacob-Chia, D. and Peter, R. (1972). Prostato-cystopexy for a paraplegic case with an inactive bladder and perineum. *Paraplegia*, **10**, 64-67.

Dollfus, P., Jurascheck, F., Adli, G. and Chapuis, A. (1976). Impairment of erection after external sphincter resection. *Paraplegia*, **13**, 290-293.

Donker, P. J., Ivanovici, F. and Noach, E. L. (1972). Analysis of the urethral pressure profile by means of electromyography and the administration of drugs. *British Journal of Urology*, **44**, 180-193.

Donovan, H. (1947). Care of the urinary tract in paraplegic patients. *Lancet*, **1**, 515-518.

Elbadawi, Ahmed and Schenk, E. A. (1974). A new theory of the innervation of bladder musculature. Part 4. Innervation of the vesico-urethral junction and external urethral sphincter. *Journal of Urology*, **111**, 613-617.

Emmett, J. L. (1940). Urinary retention from imbalance of detrusor and vesical neck: treatment by transurethral resection. *Journal of Urology*, **43**, 692-704.

Emmett, J. L. (1947). Further observations in the management of cord bladder by transurethral resection. *Journal of Urology*, **57**, 29-41.

Emmett, J. L. (1954). *Urology*, ed. M. F. Campbell, vol. 2. Philadelphia: Saunders, p. 1255.

Enhorning, G. (1961). Simultaneous recording of intravesical and intraurethral pressure. *Acta Chirurgica Scandinavica*, Supplement 276.

Gibbon, N. O. K., Ross, J. C. and Damanski, M. (1965). Bladder neck resection in the paraplegic—report of over 100 cases. *International Journal of Paraplegia*, **2**, 264-278.

Gibbon, N. O. K. (1973). Division of the external sphincter. *British Journal of Urology*, **45**, 110-115.

Haines, R. W. (1969). The striped compressor of the prostatic urethra. *British Journal of Urology*, **41**, 481-493.

Hodgkinson, C. P., Ayres, M. A. and Drukka, B. H. (1963). Dyssynergic detrusor function in the apparently normal female. *American Journal of Obstetrics and Gynecology*, **87**, 717.

Hutch, J. A. and Rambo, O. N. (1967). A new theory of the anatomy of the internal urinary sphincter and the physiology of micturition. III. Anatomy of the urethra. *Journal of Urology*, **97**, 696-704.

Jameson, R. M. (1974). Management of the bladder in non-traumatic paraplegia. *Paraplegia*, **12**, 92-97.

Linker, D. G. and Tanagho, E. A. (1975). Complete external sphincterotomy: correlation between endoscopic observation and the anatomic sphincter. *Journal of Urology*, **113**, 348-352.

O'Flynn, J. D. (1972). External sphincterotomy for the relief of outlet obstruction in neurogenic bladder. *Paraplegia*, **10**, 29-36.

Ross, J. C. (1956). Treatment of the bladder in paraplegia. *British Journal of Urology*, **28**, 14-23.

Ross, J. C. and Damanski, M. (1953). Pudendal neurectomy in the treatment of the bladder in spinal injury. *British Journal of Urology*, **25**, 45-50.

Ross, J. C., Gibbon, N. O. K. and Damanski, M. (1964). Bladder dysfunction in non traumatic paraplegia. *Lancet*, 779-782.

Ross, J. C., Gibbon, N. O. K. and Damanski, M. (1967). Division of the external sphincter in the treatment of the neurogenic bladder—a ten year review. *British Journal of Surgery*, **54**, 627-628.

Ross, J. C. and Jameson, R. M. (1971). Vesical dysfunction due to prolapsed disc. *British Medical Journal*, **3**, 752-754.

Scott, F. B. (1967). In *Neurogenic Bladder*, ed. S. Boyarsky. Baltimore: Williams and Wilkins, p. 133.

Semans, H. (1967). In *Neurogenic Bladder*, ed. S. Boyarsky. Baltimore: Williams and Wilkins, p. 133.

Tanagho, E. A. and Smith, D. R. (1966). The anatomy and function of the bladder neck. *British Journal of Urology*, **38**, 54-71.

Thomas, D. G. (1976). The effect of transurethral surgery on penile erections in spinal cord injury patients. *Paraplegia*, **13**, 286-289.

Vincent, S. A. (1966). Some aspects of bladder mechanics. *Bio-Medical Engineering*, **1**, 438-440.

Walsh, J. Personal communication.

Watkins, K. H. (1936). The bladder function in spinal injury. *British Journal of Surgery*, **23**, 734-759.

The Authors

J. Cosbie Ross, FRCS, Honorary Consultant Urologist, Regional Urological Centre, Liverpool.
N. O. K. Gibbon, FRCS, FRCSE, Head, Regional Urological Centre, Liverpool.
G. Sham Sunder, FRCSE, Commonwealth Medical Fellow in Urology, Sefton General Hospital, Liverpool.

British Journal of Urology (1976), **48**, 657-662 ©

An Assessment of Surgical Treatment of Vesical Outlet Obstruction in Spinal Cord Injury: A Review of 471 Cases

J. DERMOT O'FLYNN

National Medical Rehabilitation Centre, Dun Laoghaire, Co. Dublin, Urological Department, Meath Hospital, Dublin

Transurethral resection of the vesical neck and prostate (T.U.R.), and external sphincterotomy, used for the relief of outlet obstruction in neuropathic bladder are now well established surgical procedures. The rationale for the use of these operations is largely derived from clinical experience. Emmett and Dunn (1946), and others, noticed that patients presenting with vesical disability due to neurological disease or spinal cord injury, had disabilities very similar to those due to prostatic, and other forms of outlet obstruction, in that the bladder emptied incompletely and developed trabeculation. They found that by resecting the bladder neck and prostate in these patients, satisfactory voiding could be established.

Later, Ross, Gibbon and Damanski (1958, 1963), resected part of the external sphincter transurethrally in cases where T.U.R. had failed. They obtained good results from the operation and were able to show radiologically the presence of obstruction at the level of the external sphincter. They later modified their technique and divided the external sphincter in separate areas, using electro-cautery.

Failure to establish good voiding following T.U.R., most frequently occurs in high level spinal cord lesions, especially in thoracic and cervical lesions, and in those patients in whom spasticity is marked. The concept that the external sphincter might be the primary source of obstruction, and the vesical outlet secondary to this, was suggested; and external sphincterotomy done as a primary procedure was tried (O'Flynn, 1972). In cases where this failed, T.U.R. was done as a secondary procedure. In selected cases—*e.g.* complete cervical lesions—simultaneous external sphincterotomy and T.U.R. (a combined operation), was also tried (O'Flynn, 1974).

The success of these 2 procedures in most cases shows that the clinical evidence, on which the rationale for these operations is based, is sound; the elimination of obstruction at these 2 levels can result in satisfactory low pressure and adequate emptying of the bladder, which will protect the upper urinary tract from the effects of back pressure. These operations may have to be done more than once in the life of any patient with a static or progressive neurological lesion, and they sometimes fail to achieve their expected results.

The degree of neurological disability is never exactly reflected in the vesical disability. For example, the difference in bladder function of any 2 patients with the same level of spinal cord lesion may be great; it is well-known that some cases with, say, a complete cervical injury, may never develop outlet obstruction, whereas others do, and may need several operations to correct it. A neurological lesion that appears to be static, as occurs in spinal cord injury, does not necessarily mean that vesical disability will remain unchanged. Especially in the period immediately following spinal cord injury there may be great variation in vesical function, in the way that the normal smooth act of micturition is affected, and in the way that the neuropathic bladder behaves.

Read at the 32nd Annual Meeting of the British Association of Urological Surgeons in London, June 1976.

Table I

Level and Extent of Spinal Lesion in 471 Cases

Lesion	Complete	Incomplete	Total
Cervical	106	234	340 (72·2%)
Thoracic	53	36	89 (18·9%)
Lumbar	6	36	42 (8·9%)
Totals	165 (35·0%)	306 (65·0%)	471

Again, it is a fact that in some patients, outlet obstruction is never relieved by even repeated transurethral resection and external sphincterotomy. In these patients other factors, such as perineal muscle spasticity, which may cause lengthening and distortion of the urethra, may be the predominating feature.

So far, research has not indicated in detail how the act of micturition is disturbed, following neurological disability. There is a gap in our knowledge of the abnormal physiology of the neurologically disabled bladder, and consideration of the success or failure of T.U.R. and external sphincterotomy must be made in the context that our basic knowledge of bladder and urethral physiology is still incomplete.

In this communication the results of the operations to relieve outlet obstruction due to spinal cord injuries, done at the National Medical Rehabilitation Centre, Dun Laoghaire, are reported. This covers all the patients admitted during the years 1961 to 1974 inclusive. The gross figures inevitably include patients who died after admission, and those whose extensive disabilities prevented their being satisfactorily rehabilitated. It must be appreciated that the indications for the various procedures varied with the experience obtained in dealing with these cases, and modifications in approach were dictated by this, and by the results reported in other paraplegic units.

The indications for these operations are based on the present theory that the 2 main sources of outlet obstruction in neuropathic bladder are the external sphincter and the vesical neck, or internal urinary orifice. In the treatment of the patients reported here, these procedures were used either alone, or in sequence, or as a combined operation, to relieve outlet obstruction. Urinary diversion was only carried out when this was not possible. No rehabilitated patient was allowed home with a urethral catheter *in situ*, but some of those who had to remain hospitalised continued on catheter drainage. Diversion was also done in female patients where persistent incontinence was the main indication. In a few of the earlier cases in the series pudendal neurectomy had been done, but the results of this operation were unsatisfactory.

The technique for T.U.R. was exactly the same as for prostatic resection, the aim of the operation being to remove all the tissue from the internal urinary orifice to the verumontanum. Limited vesical neck resection or posterior lip resection have not been done in this series. Most of the external sphincterotomies were done using 4 cuts in the external sphincter at 2, 4, 8 and 10, but in some of the earlier cases a lesser number of incisions were made (O'Flynn, 1972).

Of a total of 471 consecutive new cases of spinal cord injury admitted to the centre, 139 (29·5%), developed outlet obstruction for which surgery was necessary. The level and extent of the spinal lesions are shown in Table I. Because of the changing concepts of treatment, different methods were tried at different periods. Initially, in 1961, it was accepted that T.U.R. was the first operation for the relief of outlet obstruction. In 1966 external sphincterotomy was introduced for the failed T.U.R. The next development, in 1969, was the use of external sphincterotomy as the

Table II

Initial Operations for Vesical Outlet Obstruction in 139 Cases

T.U.R.	93 (66·9%)
External sphincterotomy	28 (20·2%)
Combined operation (T.U.R. and external sphincterotomy)	16 (11·5%)
Urinary diversion	2 (1·4%)

primary operation, especially in cervical lesions, where the external sphincter might be expected to be the chief cause of outlet obstruction; but in a further group, where the operation failed, a T.U.R. was done as a secondary procedure. Recently, since 1971, for some cases—mostly cervical lesions—external sphincterotomy and T.U.R. have been done at the same time (*i.e.* a combined operation). The initial procedure used for outlet obstruction, as the result of this programme, is shown in Table II.

The completeness of the spinal cord lesion and its level are of some importance in relation to the development of vesical outlet obstruction. The details are seen in Table III; it is interesting to note that thoracic lesions demand outlet operations more frequently than cervical or lumbar lesions. As might be expected, operations are more frequently necessary in complete lesions, than in incomplete lesions.

Table III

Vesical Outlet Obstruction with Spinal Cord Injuries: 471 Cases

	Number with operation for vesical outlet obstruction		
Lesion	Complete	Incomplete	Total
Cervical (340 cases)	49	25	74 (21·8%)
Thoracic (89 cases)	42	12	54 (60·7%)
Lumbar (42 cases)	6	5	11 (26·2%)
Total	97	42	139

The indications for these procedures were usually multiple, but one or more of the following conditions, which might co-exist at the same time, were considered mandatory.

1. Persistent difficulty in initiating and maintaining the urinary stream.
2. Inadequate bladder emptying and failure to achieve a "balanced bladder".
3. Persistent urinary infection, associated with a high residual urine (*i.e.* over 120 ml).
4. Radiographic evidence of upper urinary tract obstruction (*i.e.* ureterectasis or pyelectasis).

The method of management was to carry out the primary procedure on the patient, and to re-assess voiding and emptying carefully in the succeeding weeks after operation, and then at varying intervals from 3 to 6 months, depending on what were the clinical indications. From this it was found that secondary operations were frequently necessary, usually within a year

Table IV

Spinal Cord Injuries: Secondary Procedures per Year

Year	T.U.R.	Ext. Sph.	Combined	Total
1	37	21	5	63
2	4	4	3	11
3	7	5	1	13
4	3	2	0	5
5	0	2	0	2
6	0	1	0	1
7	1	0	0	1
8	0	2	1	3
9	0	1	0	1
10	1	0	0	1

after a primary operation had been done, but thereafter operations for outlet obstruction were rarely required (Table IV).

The initial operation to relieve outlet obstruction in neuropathic bladder frequently fails to achieve its objective. It was noted by Emmett and Beare (1948), that repeated T.U.R. was frequently necessary to get a good result. It is also now evident that external sphincterotomy may also need to be repeated. Various reasons may be adduced for this. For instance, the pathological physiology of outlet obstruction is not clearly understood, the operations themselves may be inadequate, or the technique faulty, changes may take place in the bladder neck of which there is no clear understanding, changes in neurological lesions—although frequently minimal—may also occur, and also there is undoubtedly great variation in the way the bladder functions for some months, at least, after a spinal cord injury.

Secondary or Repeat Operations

Of 139 cases requiring primary operations for outlet obstruction, secondary or repeat operations were necessary in 72 patients, when the initial operation failed to achieve its objective (Table V).

Table V

Secondary Operations for Vesical Outlet Obstruction

Initial operations	139 patients
Secondary operations (1 or more)	72 patients
After initial T.U.R.	55·9%
After initial ext. sphinct.	53·6%
After initial combined op.	31·2%

This generally meant that the patient failed to void, or to empty the bladder satisfactorily. The type of secondary operation chosen depended on the anticipated prognosis for bladder function. Where a "balanced bladder" with good urinary control was anticipated, as might be expected in low and incomplete lesions, the initial operation was repeated. It should be observed that T.U.R. alone, or external sphincterotomy alone, do not necessarily cause total incontinence,

Table VI

Secondary Operations for Vesical Outlet Obstruction: Level of Cord Injury

Level	Complete	Incomplete	Total
Cervical	29	11	40 (55·6%)
Thoracic	24	3	27 (37·5%)
Lumbar	3	2	5 (6·9%)
Total	56	16	72

but—if it should be desired—T.U.R. and external sphincterotomy done in sequence, or as a combined operation, will usually do so.

It is also evident that the level and extent of the spinal cord lesion is related to the likelihood of a repeat operation being necessary (Table VI). From these figures it can be seen that secondary procedures are more likely to be necessary in complete and in high level lesions; 29 (59%) of 49 complete cervical lesions, 24 (57%) of 42 complete thoracic lesions, and 3 (50%) of 6 complete lumbar lesions, required a secondary operation.

Changes in policy may be reflected in these figures, for example, early external sphincterotomy for complete cervical lesions, was not as effective as expected.

There was no mortality associated with these operations.

In the whole series a total of 6 urinary diversions—2 suprapubic cystostomies, 2 cutaneous vesicostomies, 1 cutaneous ureterostomy, and 1 ileal loop diversion—were done in cases where outlet operations had failed, or for uncontrollable incontinence in females.

No detailed analysis has been made of the 68 (17%) female patients in this series. Operations for outlet obstruction were necessary in 11 patients (16%), and 3 of these (27%) required further operations; 2 patients needed a urinary diversion. Following the expected pattern, 9 (82%) of the patients requiring operation had complete spinal cord lesions.

Discussion

This study confirms that operations on the vesical neck and external sphincter are successful in the treatment of vesical outlet obstruction following spinal cord injury, and this conclusion is supported by the fact that only a small number (6) of the patients in the series, needed a urinary diversion.

The indications for the use of the individual operations have been discussed elsewhere (O'Flynn, 1974). Generally, it may be said of this series, that the lower and more incomplete lesions were treated by T.U.R., and the higher and complete lesions by external sphincterotomy; when neither operation achieved its objective, further operation—either a repeat of the original one, or the use of the other in sequence, or combined—was done. The results of this policy have been satisfactory in that the vast majority of the cases have been made catheter-free.

What is difficult to explain is the high incidence of repeat operations. All the operations were done by standard technique, and some technical difficulties have been noted. A satisfactory resection in a young male spinal cord injuries patient should produce 5-7 g of tissue, but in doing a radical resection, sinuses are frequently opened, and may lead to hasty termination of the procedure, although in practice this has rarely occurred. If at a subsequent procedure any tissue (no matter how small an amount), was resected, it was recorded as a repeat T.U.R. External sphincterotomy is usually an easy procedure, if done after a T.U.R. When it is done as a primary procedure the area of the sphincter frequently becomes distorted after the first incision is made, subsequent incisions can then be difficult to do, and may not be of the correct depth and length. Endoscopic examination in some of these patients has shown what appears to be a normal sphincteric area, suggesting either that the original operation was incomplete, or that there was reformation of the sphincter; but in most patients the now epithelialised incisions are clearly seen.

Probably the most significant fact is that the majority of the repeat operations were done in the first year after the initial procedure. This may reflect the great variation in function of the detrusor and vesical outlet musculature which follows spinal cord injury; possibly the operations would be more definitive if they could be delayed until the bladder outlet function has stabilised. This would have great practical disadvantages, however, since the patient would be on catheter drainage for a longer period, with the chance of more complications arising from urinary tract infections. With the absence of any mortality or morbidity following these operations no immediate change in the policy of doing repeat operations is indicated, but the necessity for continued study of bladder function in the spinal cord injury patient is obvious.

Summary

An assessment of 139 cases of outlet obstruction following spinal cord injury, in a consecutive series of 471 patients, is presented.

The figures in relation to the level and extent of the spinal lesion and the type of operation (transurethral resection and external sphincterotomy), are reviewed.

The incidence of repeat operation is recorded and assessed.

It is concluded that transurethral resection and external sphincterotomy, either alone or combined, will relieve outlet obstruction in most cases of neuropathic bladder following spinal cord injury.

References

Emmett, J. L. and Beare, J. B. (1948). Transurethral resection for vesical dysfunction in cases of tabes dorsalis. *Journal of the American Medical Association*, **136**, 1093-1096.

Emmett, J. L. and Dunn, J. H. (1946). Transurethral resection in the surgical management of cord bladder. *Surgery, Gynecology and Obstetrics*, **83**, 597-612.

O'Flynn, J. D. (1972). External sphincterotomy for the relief of outlet obstruction in neurogenic bladder. *Paraplegia*, **10**, 29-36.

O'Flynn, J. D. (1974). Neurogenic bladder in spinal cord injury. *Urologic Clinics of North America*, **1**, 155-162.

Ross, J. C., Gibbon, N. O. K. and Damanski, M. (1958). Division of the external urethral sphincter in the treatment of the paraplegic bladder. *British Journal of Urology*, **30**, 204-212.

Ross, J. C., Gibbon, N. O. K. and Damanski, M. (1963). Further experiences with division of the external urethral sphincter in the paraplegic. *Journal of Urology*, **89**, 692-695.

The Author

J. Dermot O'Flynn, MCh, FRCSE, FRCSI, Lecturer in Urology, Trinity College, Dublin, Consultant Surgeon, Urological Department, Meath Hospital, Dublin.

British Journal of Urology (1976), **48**, 663-670 ©

Urodynamics in the Prune Belly Syndrome

H. M. SNYDER, N. W. HARRISON, H. N. WHITFIELD and D. INNES WILLIAMS
Shaftesbury Hospital and the Institute of Urology, London

There have been many descriptions of the triad which constitutes the prune belly syndrome: agenesis of the abdominal wall musculature, bilateral undescended testes and dysmorphic changes in the urinary tract (Williams, 1974). There is, however, little information available describing the functional characteristics of the syndrome. The intravenous pyelogram and the micturating cystogram often show a very disturbing picture of dilated and tortuous ureters (Fig. 1). In some children this picture is accompanied by progressive ureteric dilatation, infection, and loss of renal function, but in others it is present for many years with few if any symptoms and stable function.

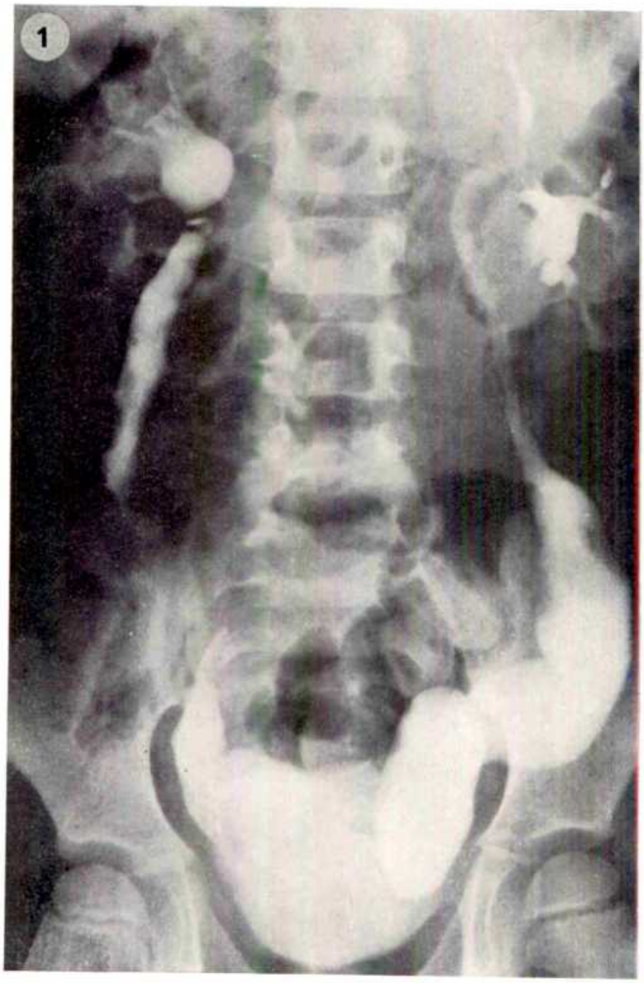
It is often difficult to determine not only when to intervene surgically but also which part of the urinary tract to treat. There has been enthusiasm in some centres for extensive remodelling and re-implantation of the upper tracts. While recognising that this is sometimes necessary, we have noted considerable upper tract improvement in some cases by treating the area of apparent obstruction just below the verumontanum (Fig. 2) by urethrotomy and thus producing better bladder emptying. This finding which has been confirmed by others (Cukier, 1976) stimulated us to look into the urodynamics of the prune belly syndrome with hope of not only beginning to characterise the functional defect in this syndrome but also of finding urodynamic parameters which might assist in planning the surgical management of these children.

Methods

There were 10 boys or young adults aged 5 to 27 years with the prune belly syndrome among those being followed at the Hospital for Sick Children, Great Ormond Street, and at the Shaftesbury Hospital available for study (Table). No child with a urinary diversion was included and boys less than 5 years of age were excluded as urodynamic investigations are difficult in the very young.

The urethral pressure profile was carried out by the modification of the Brown and Wickham (1969) method previously described from the Institute of Urology (Harrison and Constable, 1970). The cystometrogram was carried out by gravity filling (approx. 100 ml/min) of the bladder with saline while continuously monitoring intrinsic bladder pressure (total bladder pressure minus rectal pressure) by means of a 1 mm epidural catheter placed alongside the filling catheter. With the filling catheter removed bladder pressure and flow were recorded during voiding. When feasible a combined radiographic pressure/cystogram was carried out after the manner of Bates and Corney (1971). Upper urinary tract pressure/flow studies were carried out in 1 boy by the technique described by Whitaker (1973).

Read at the 32nd Annual Meeting of the British Association of Urological Surgeons in London, June 1976.



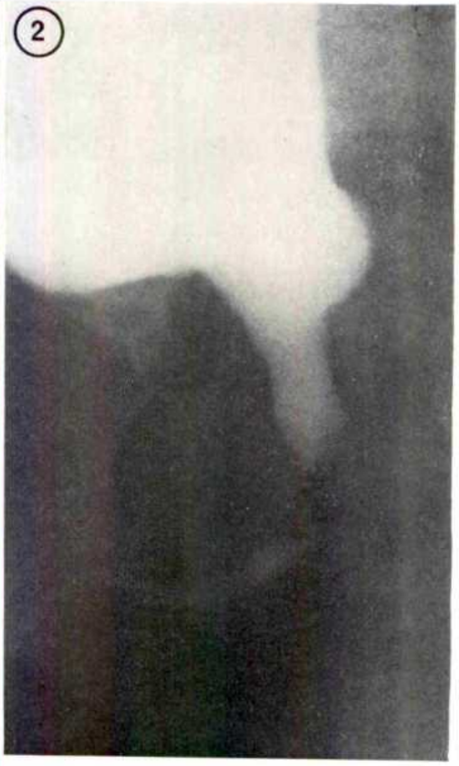


Fig. 1. Intravenous urogram in a boy aged 5 with typical upper tract features of the prune belly syndrome.

Fig. 2. Micturating cystogram in the same boy as Figure 1 showing characteristic wide posterior urethra tapering to just below the verumontanum.

Results (see Table)

The Urethral Pressure Profile

Only 3 boys in this study had never had any urethral surgery. In these the maximum resting urethral pressure (Case 1—65 cm H_2O, Case 2—44 cm H_2O, Case 3—45 cm H_2O) was in the normal to low range for their age (normal 60-120 cm H_2O (Harrison, 1971)). 3 other boys were studied only after a urethrotomy had been carried out. In them the maximum resting pressure was on the low side of normal (Case 8—45 cm H_2O, Case 9—45 cm H_2O, Case 10—38 cm H_2O). Of the 3 boys having urethral pressure profiles done pre- and post-urethrotomy, 1 (Case 6) had at the first examination a resting pressure on the low end of the normal range at 60 cm H_2O. The other 2, however, had pressures on the high end of the normal range (Case 4—120 cm H_2O,

Table

Urodynamics in Prune Belly Syndrome

						Cystometrogram: voiding phase					
		Urethral pressure profile Max. pressure (cm H_2O)		Cystometrogram: filling phase		Max. flow (ml/sec)		Voiding pressure (cm H_2O)		Residual vol. (ml)	
		Urethrotomy				Urethrotomy		Urethrotomy		Urethrotomy	
No.	Age (yr)	Pre	Post	Filling vol. (ml)	End filling pressure (cm H_2O)	Pre	Post	Pre	Post	Pre	Post
1	12	65 cm H_2O	No surg.	800 cc	0	25 cc/s	No surg.	45 cm H_2O	No surg.	17 cc	No surg.
2	11	44	No surg.	800	10	33	No surg.	40	No surg.	5	No surg.
3	5	45	No surg.	920	15	12	No surg.	50	No surg.	250	No surg.
4	20	120	62	2,100	0	5	13	70	35	850	600
5	27	–	–	600	0	40	–	110	–	50	–
6	15	60	25	600	5	10	15	45	–	2,500	425
7	8	115	60	750	20	22	22	–	50	60	65
8	14	–	45	2,000	30	–	30	–	70	–	130
9	15	–	45	800	5	–	–	–	–	–	0
10	17	–	38	1,600	0	–	23	–	20	3,500	105

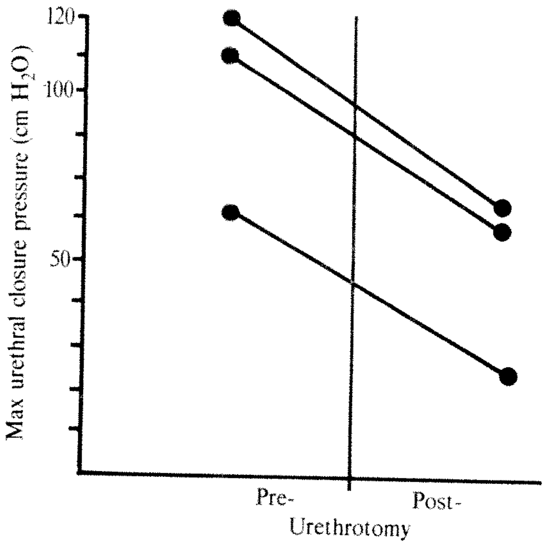


Fig. 3. Urethral closure pressures before and after urethrotomy.

Case 7—115 cm H_2O). In all 3 the post-urethrotomy resting pressures were reduced by approximately 50% (Fig. 3).

The Cystometrogram: Filling Phase

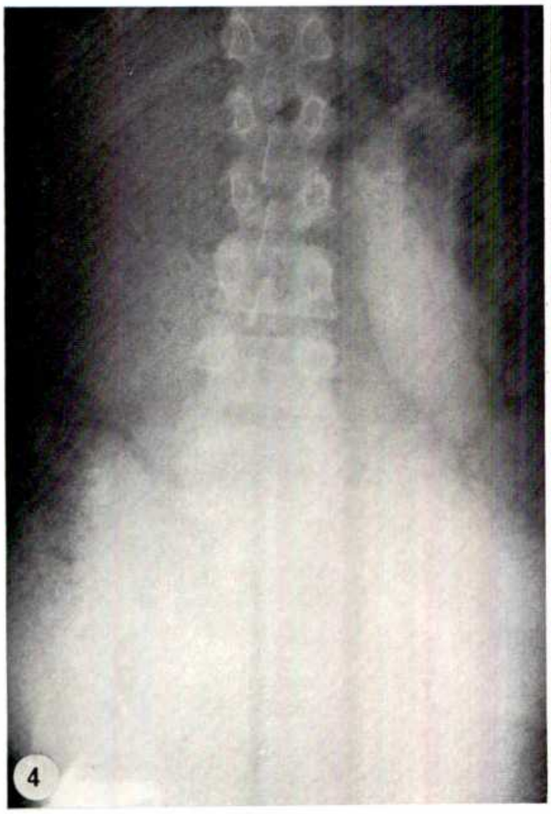
As might be expected from the large bladders so often seen on cystogram, the filling phase is markedly shifted to the right. Average first sensation took place at 930 cc (normal 150-250 ml) and average filling volume was 1,097 cc (normal 250-550 ml).

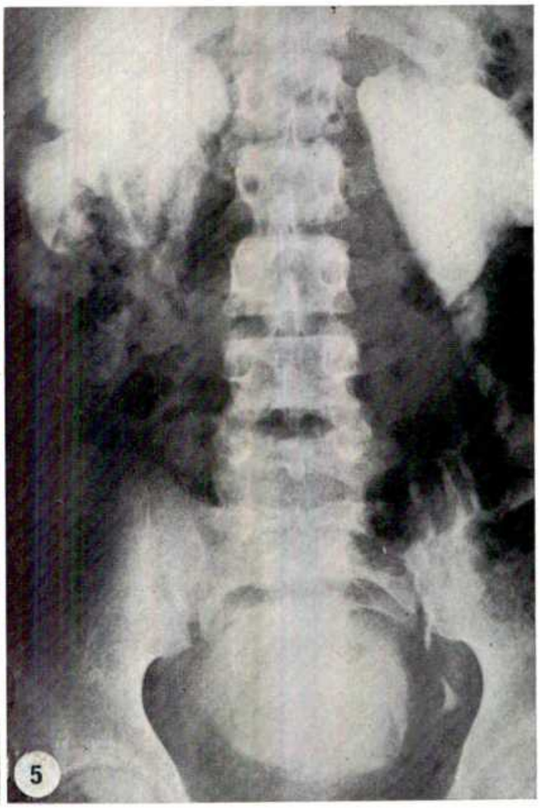
In 3 boys (Cases 2, 3 and 7) unstable contractions were noted during filling. As the voiding pressure was normal this instability was not likely to have been caused by outflow obstruction. 1 boy (Case 3) was incontinent during unstable contractions provoked by rapid filling. Slower filling provoked much less unstable activity and no incontinence. None of the 3 gave any history of urinary incontinence.

End filling pressure ranged from 0 to 30 cm H_2O but only 2 (Cases 7 and 8) had an end filling pressure above 15 cm H_2O. The 3 cases with unstable bladders had end filling pressures which were among the higher values (10, 15 and 20 cm H_2O).

The Cystometrogram: Voiding Phase

Pressure flow data show that the typical bladder morphology seen in the prune belly syndrome is compatible with normal function (Cases 1, 2 and post-urethrotomy Cases 7 and 8). In Case 5 the voiding pressure (110 cm H_2O) was high (normal 69·4 ± 30·6 cm H_2O (Gierup, 1970*a*), indicating that the detrusor was able to raise intravesical pressure and maintain a good urine flow. The residual in this case was small. 3 cases had a low flow rate (normal 14-34 ml/s (Gierup, 1970*b*)) with normal voiding pressure (Case 3—12 ml/s at 50 cm H_2O; Case 4 preurethrotomy—5 ml/s at 70 cm H_2O; Case 6 preurethrotomy—10 ml/s at 45 cm H_2O). All 3 had significant residuals (Case 3—250 cc; Case 4—850 cc; Case 6—2,500 cc). Cases 4 and 6 underwent a urethrotomy which produced an increased flow (Case 4 from 5 to 13 cc/s; Case 6 from 10 to 15 ml/s) and a drop in maximum voiding pressure (Case 4 from 70 to 35 cm H_2O). In both cases the residual decreased (Case 4 from 850 to 600 cc; Case 6 from 2,500 to 425 cc). Case 10 following urethrotomy





Figs. 4 and 5. Intravenous urogram before and 3 months after urethrotomy showing improvement in the upper urinary tracts (Case 10).

had a low voiding pressure (20 cm H_2O) associated with a normal flow (23 cc/s) and a small residual.

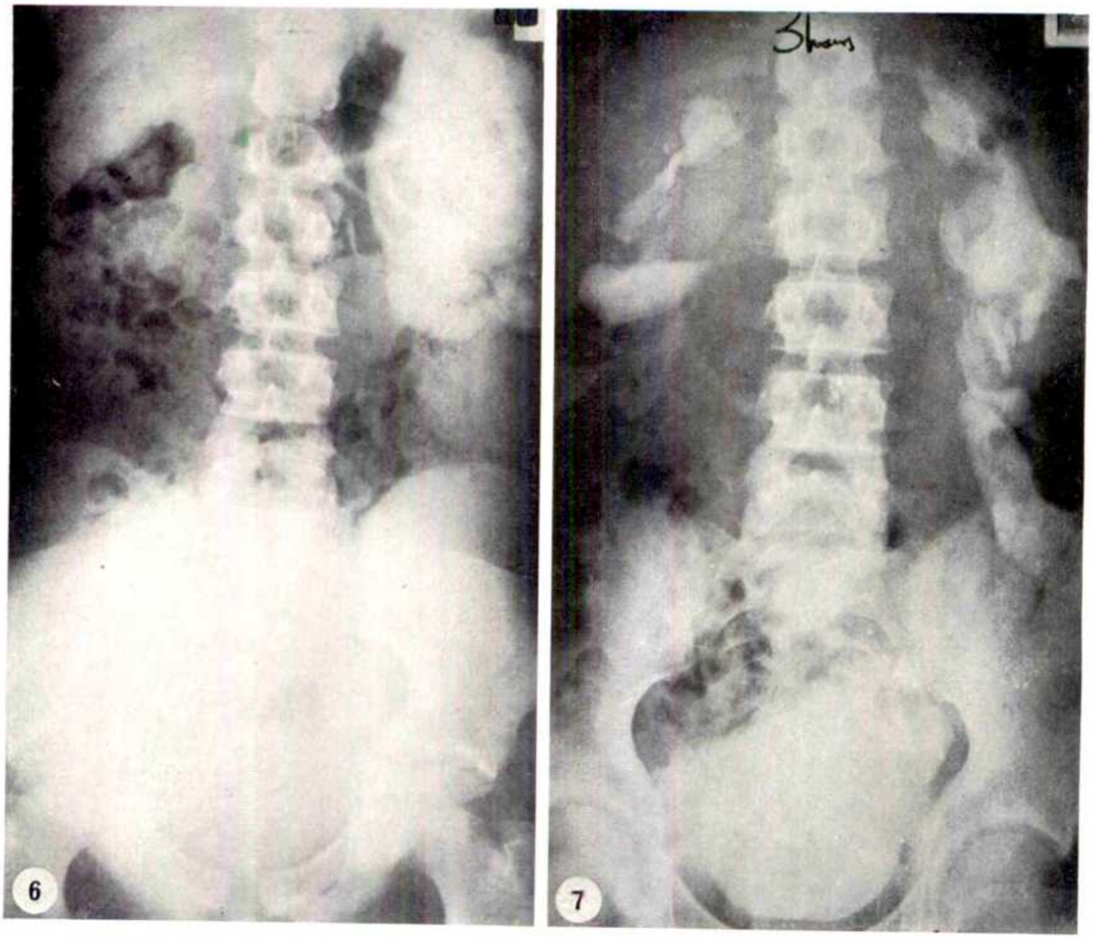
Upper Tract Pressure/Flow Studies

In 1 boy with the typical ureteric changes seen in the prune belly syndrome (Fig. 1) we carried out ureteric puncture and pressure/flow studies at the time of orchidopexy. At an infusion rate of 10 cc/min there was only a 10 cm H_2O pressure rise in the ureter.

Discussion

The dilated and tortuous urinary tract seen in the prune belly syndrome readily gives the impression that function must also be abnormal. It should be emphasised, however, that this picture is compatible with normal function. The large capacity bladder so often present may be capable of emptying well (Cases 1, 2 and 5, and post-urethrotomy Cases 7, 8, 9 and 10). Thus the presence of a large bladder alone need not imply an unbalanced voiding mechanism nor need for intervention.

It appears likely that voiding dynamics in the prune belly syndrome have a greater tendency to become unbalanced than in the normal population. The subsequent development of a large residual may in turn have adverse effects on the upper tracts. Efforts to lower outflow resistance



Figs. 6 and 7. Intravenous urogram in another boy (Case 6) before and 3 months after urethrotomy.

by urethrotomy as we have done, or perhaps by an α-blocker such as phenoxybenzamine may lead to a return of balanced voiding, decreased residuals and upper tract improvement.

Voiding studies provide an insight into the nature of the unbalanced dynamics present and can contribute to management. If a low flow rate and sizeable residual urine are associated with a normal voiding pressure (Case 3 and preurethrotomy Cases 4 and 6), then this indicates a decompensated detrusor unable to overcome the outflow resistance present. Intervention to lower urethral resistance is reasonable. Case 3, the youngest boy in our series, had absolutely no symptoms and therefore it was elected merely to follow him closely. Cases 4 and 6 complained of a slow stream; so slow in Case 6 that he had to sit to void. In each a urethrotomy was carried out. Both boys reported improved streams and this was confirmed by increased flow rates and lower voiding pressures. The residuals are now smaller in both cases but are still significant and careful follow-up is indicated. In general it would appear that an effort to lower urethral resistance can be recommended as an early and simple step in treating the decompensated detrusor.

If the flow rate is normal and the residual is small, this usually indicates acceptable balanced voiding dynamics. However, if this is achieved by a compensated detrusor producing a high voiding pressure then there may be potential for trouble such as infection (Lapides, 1965).

Case 5 developed just such a situation with recurrent infection and flank pain. A urethrotomy improved his symptoms. Follow-up urodynamics have not yet been performed. On the basis of such limited experience it is hard to make recommendations, but it would appear reasonable to perform a urethrotomy for the balanced but high pressure system which is associated with symptoms. Asymptomatic cases warrant close follow-up.

The urethral pressure profile does not necessarily reflect the resistance of the urethra during voiding and therefore by itself is unlikely to help determine which boys will benefit from urethrotomy. The urethral profile may be a guide to the adequacy of urethrotomy by observing the individual fall in pressure following the procedure. A very low pressure (less than 25 cm H_2O) is usually associated with incontinence due to sphincter deficiency (Harrison, 1971) and we would be very cautious in performing further urethral surgery in a boy whose profile was very low but who was still exhibiting inadequate emptying after urethrotomy (*e.g.* Case 6). In these circumstances an alternative procedure such as bladder plication would be more appropriate.

As has been pointed out by Whitaker (1973) a wide ureter without reflux need not be obstructed. This point is particularly relevant in the prune belly syndrome where the dysmorphic ureters are often wide and tortuous. While recurrent infection in a wide non-refluxing ureter may constitute an indication for ureteric remodelling, we feel the child with sterile urine should have obstruction demonstrated before undertaking surgery. Case 3 has a dilated ureter but no obstruction and has been stable without ureteric surgery.

While it is difficult to draw firm conclusions from a study of a group as small as the one we examined, we feel that urodynamic evaluation can have a significant role in the management of children with the prune belly syndrome. As it is not feasible to carry out a full urodynamic evaluation repeatedly in routine follow-up care, a selection of the most useful screening studies must be made. Although it is desirable to avoid instrumentation in these children, a residual urine determination is one of the most useful parameters. Residual urine determination by ultrasound (Harrison, Parks and Sherwood, 1976) may provide a satisfactory, non-invasive technique. Urine flow rates also can be measured by simple non-invasive techniques. These 2 studies we feel should be employed in the routine follow-up of boys with the prune belly syndrome. The presence of symptoms, low flow rate or significant residual urine should constitute indications for a more complete evaluation. As virtually all boys with the prune belly syndrome come to micturating cystography at some point, a case can be made for doing this routinely as a combined radiographic pressure/flow study. The asymptomatic high pressure bladder can be detected and this study will form a baseline for comparison with later studies.

As initially stated it was the notable upper tract improvement which we have seen following urethrotomy which stimulated this investigation. 2 of the boys studied (Cases 6 and 10) exemplify this point well (Figs. 4-7).

Summary

Urodynamic studies have been carried out in 10 boys with the prune belly syndrome.

In spite of gross radiological changes the condition is compatible with normal voiding dynamics. Filling cystometrograms show a marked shift to the right. Pressure/flow studies may demonstrate an unbalanced voiding mechanism which can be treated by urethrotomy.

Following urethrotomy urethral pressure profiles showed a significant fall, flow rates increased and residual urine volumes were reduced.

Urological treatment in the prune belly syndrome should be directed at producing a bladder which empties well: a balanced voiding mechanism. Urodynamic investigations are helpful in achieving this aim.

Residual urine determination and flow rates should be used in routine follow-up.

Urethrotomy to lower bladder outflow resistance is advocated as one of the first steps in treating the unbalanced voiding mechanism that is often found in the prune belly syndrome.

References

BATES, C. P. and CORNEY, C. E. (1971). Synchronous cine/pressure/flow cystography: a method of routine urodynamic investigation. *British Journal of Radiology*, **44**, 44-50.

BROWN, M. and WICKHAM, J. E. A. (1969). The urethral pressure profile. *British Journal of Urology*, **41**, 211-217.

GIERUP, J. (1970*a*). Micturition studies in infants and children. Intravesical pressure, urinary flow and urethral resistance in boys without intravesical obstruction. *Scandinavian Journal of Urology and Nephrology*, **4**, 217-230.

GIERUP, J. (1970*b*). Micturition studies in infants and children. Normal urinary flow. *Scandinavian Journal of Urology and Nephrology*, **4**, 191-207.

HARRISON, N. W. and CONSTABLE, A. R. (1970). Urethral pressure measurement: a modified technique. *British Journal of Urology*, **42**, 229-233.

HARRISON, N. W. (1971). Urinary incontinence: a clinical study of electronic methods of control. MD Thesis, University of London.

HARRISON, N. W., PARKS, C. and SHERWOOD, T. (1975). Ultrasound assessment of residual urine in children. *British Journal of Urology*, **47**, 805-814.

LAPIDES, J. (1965). Role of hydrostatic pressure and distension in urinary tract infection. In *Progress in Pyelonephritis*, ed. E. H. Kass. Philadelphia: Davis.

WHITAKER, R. H. (1973). Methods of assessing obstruction in dilated ureters. *British Journal of Urology*, **45**, 15-22.

WILLIAMS, D. I. (1974). The prune belly syndrome. In *Urology in Childhood.* Heidelberg: Springer Verlag.

The Authors

H. M. Snyder, MD, Clinical Fellow.

N. W. Harrison, MD, FRCS, Senior Registrar.

H. N. Whitfield, FRCS, Research Fellow (now Senior Registrar, Department of Urology, St Bartholomew's Hospital).

D. Innes Williams, MD, MChir, FRCS, Consultant Urologist and Dean.

Requests for reprints to: N. W. Harrison, Institute of Urology, 172 Shaftesbury Avenue, London WC2.

British Journal of Urology (1976), **48**, 671-674 ©

Anterior Detrusor Tube Repair for Urinary Incontinence in Children

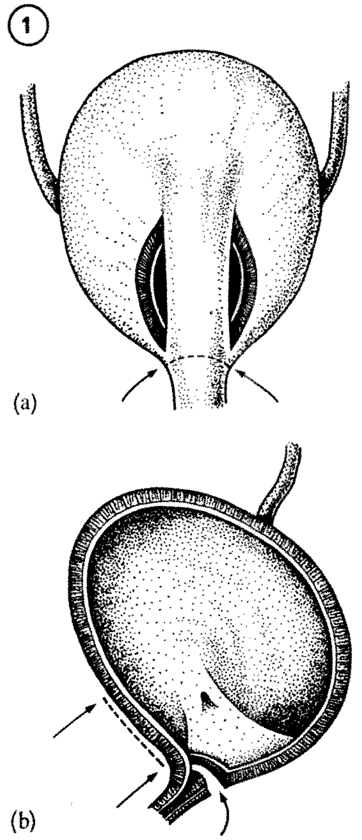
D. INNES WILLIAMS and HOWARD SNYDER
The Hospital for Sick Children, Great Ormond Street, London

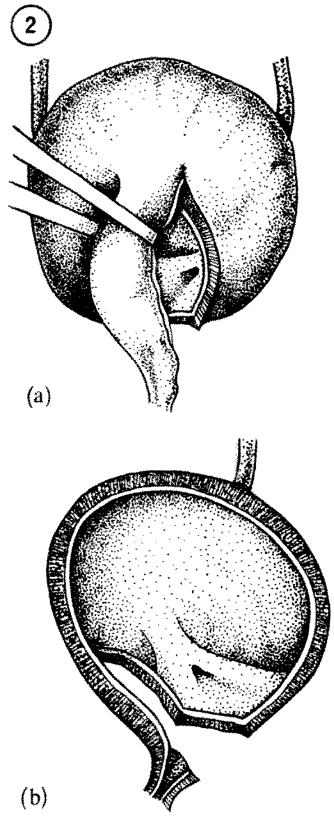
Urinary incontinence due to a deficiency of the sphincter mechanism continues to be a major clinical problem in childhood. Most often it is congenital in origin and epispadias and exstrophy form the largest group. There is, however, a further series of congenital abnormalities involving some form of urogenital sinus or a short wide urethra with deficient bladder neck, often with bilateral single ectopic ureters. The sphincter muscles may also be destroyed following trauma and we have had a number of cases where the bladder neck mechanism as well as the external sphincter was irreparably damaged following rupture of the posterior urethra in association with fracture of the pelvis. Surgical trauma to the sphincter mechanism may also result from ill-advised bladder neck revision or during the treatment of urethral valves. In the majority of these children reconstructive surgery cannot hope to reconstitute any normal sphincteric mechanism, which is absent or destroyed. Surgery may aim to bolster the scanty existing muscular tissue, or create a urethral resistance by constructing a urethral tube of sufficient length and with a tension in its wall appropriate to the calibre of its lumen to prevent the escape of urine from the relaxed bladder. It must, of course, be established that the detrusor contractions are adequate to overcome this resistance and that normal voiding patterns with cortically initiated and inhibited detrusor contractions are possible. It may be that ultimately the implantation of mechanical devices to compress the urethral tube will prove most effective, but there is evidently considerable advantage in using the normal tissues for this purpose.

Young (1908) was the first to treat successfully incontinence due to sphincter weakness by increasing urethral resistance. He suggested tightening the bladder neck and imbricating local tissues over the area of the external sphincter to reduce the lumen to the size of a silver probe. It remained to Dees (1949) to create a urethral tube out of the posterior wall of the bladder in order to provide a substitute sphincter. In 1964, Leadbetter, also Michener, Thompson and Ross (1964) reported modifications of Dees' technique, allowing a lengthier urethra made possible by re-implanting the ureters at higher level. The use of the anterior bladder wall to lengthen the urethra was introduced by Flocks and Culp (1953) in order to bridge the gap following radical prostatectomy. Tanagho *et al.* (1969) described the creation of an anterior tube for the treatment of incontinence.

It has seemed to us that both anterior and posterior tubes have a role in the treatment of urinary incontinence in children. In certain clinical settings the use of anterior bladder wall will be inappropriate: in children with exstrophy or epispadias the primary defect is anterior so that for this group of anomalies some modification of the Young Dees procedure may seem most appropriate. Similarly where there has been extensive midline anterior bladder surgery, replacement of the muscle layer by scar tissue would render this unsuitable for a reconstructive tube. In other circumstances, however, an anteriorly based reconstruction has advantages. The heavy

Read at the 32nd Annual Meeting of the British Association of Urological Surgeons in London, June 1976.





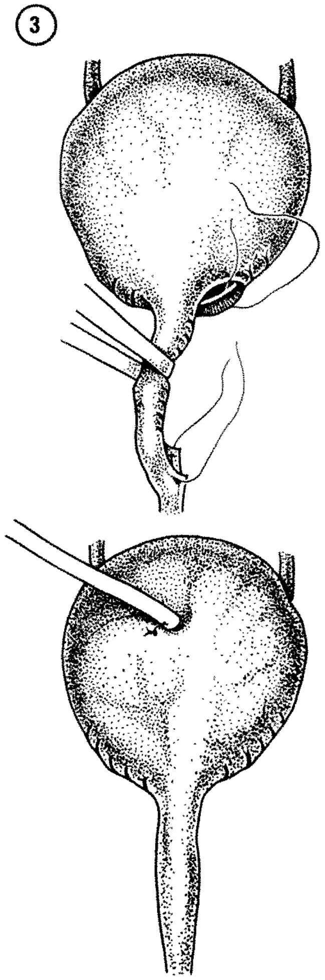


Fig. 1. A, Anterior view. B, Sagittal section showing the outlining of the anterior detrusor strip in continuity with the bladder neck.

Fig. 2. A, Anterior view. B, Sagittal section. Mobilisation of the strip and upward displacement of the trigone.

Fig. 3. Tubularisation of the strip, closure of the lateral extensions and insertion of surprapubic tube.

concentration of transversely orientated muscle fibres in the middle coat of the bladder just above the internal meatus seems to offer the possibility of elastic support comparable to that of the trigonal musculature. The avoidance of the need for ureteric re-implantation is also an advantage and where the primary pathology involves the posterior wall as in urogenital sinus, after inappropriate treatment of ectopic ureterocele, or after wedge resection of the bladder neck, the possibility of avoiding the damaged rigid posterior structures and creating an elastic resistance from pliable anterior tissue at a higher level has considerable appeal. It must be emphasised that in all cases, it is necessary for the bladder to be of adequate capacity and capable of strong contractions without evidence of instability.

Technique

Our procedure is a modification of that described by Tanagho *et al.* (1969). The abdomen is opened through a Pfannenstiel incision, holding stitches are placed in the anterior bladder wall and the bladder is opened by a vertical incision, somewhat to one side of the midline. After inspection of the interior of the bladder and the condition of the sphincter mechanism, the anterior bladder strip (2-3 cm wide) is then defined by placing 2 more holding sutures and making a parallel incision down to the bladder neck (Fig. 1). This strip is now held forward so that the bladder neck can be visualised and the posterior arc of the neck is divided through all layers (Fig. 2). The plane posterior to the bladder is easily opened up and the trigonal area mobilised so that it can be drawn upwards. There is thus an anterior bladder strip with continuity at both ends and therefore a good blood supply. The strip is formed into a tube by a continuous chromic catgut suture from the distal point of the strip at the old bladder neck, upwards for a distance of 3 or 4 cm (Fig. 3). Reconstitution is carried out over 10 Ch. catheter, threaded up through from the urethra. The midpoint of the trigone is then sutured to the apex of the tube which has just been created. This leaves a "dog ear" on each side, which is closed by 2 continuous layers of chromic catgut suture. A Malecot catheter is placed in the dome of the bladder and if there is any danger that the ureteric orifices have been left too close to the lateral closure they also may be intubated. The peritoneum is then opened beside the bladder and the omentum mobilised sufficiently to wrap around the tube. This serves both to fill the dead space and to maintain the elasticity of the tube. The anterior bladder wall is then suspended from the posterior aspect of the rectus muscle to prevent collapse or kinking. The wound is closed with a pre-vesical drain. The urethral catheter is removed after 2 weeks and the suprapubic then clamped for a trial of voiding. At first there is apt to be some residue but this has been reduced in a short time.

Complications and Results

The only serious complication of this operation has been retention, apparently due to the ridge at the new bladder neck and the creation of a "retort" type of anatomy. This has required a dilatation in 2 and revision in 2. Several of the successful cases are apt to suffer from episodes of infection and this may be due to very small volumes of residual urine.

The analysis of results is complicated by the diverse nature of the original pathology. There were 4 examples of urogenital sinus with absence of formation of a bladder neck at the junction between the bladder and vaginal area. 3 of these cases became continent, though with occasional nocturnal enuresis, 1 had a slight improvement and then became obstructed and is at present undergoing revision. There were 4 cases which may be described in general as having a wide bladder neck and short urethra. In the first, the child had had 2 previous attempts at posterior repair by the Young Dees procedure leaving a completely rigid urethral tube. The anterior reconstruction leaving the fibrotic area below it resulted in a very satisfactory diurnal continence. A second case at first failed to improve, was then tightened a little and went into retention, but has now been given normal diurnal control by a further bladder neck revision. 1 case with a single ectopic ureter, failed altogether so that diversion has been required. 1 girl has such frequency, although she no longer dribbles, that she can hardly be counted a success.

In 1 example an ectopic ureterocele had been treated in early infancy by extensive surgery leaving an entirely deficient posterior bladder neck and urethral wall. She was a very fat pubertal child in whom the possibilities of local reconstruction seemed too formidable and the anterior tube was undertaken leaving the deficient area untouched. She had a very satisfactory result.

There were 3 cases in which a fractured pelvis with a ruptured urethra had been repaired by urethroplasty but had left the child totally incontinent by day. The origin of the bladder neck defect in these was not always clear; in them the original injury had taken place when they were under the age of 5 years and it may be that direct trauma was responsible at an age when the upper part of the urethra and bladder neck were unprotected by any prostatic tissue. There was a further possibility that an indwelling Foley catheter, with the application of traction, had led to ischaemic damage to the bladder neck tissue. At all events the bladder neck in these boys was rigid and widely open. The anterior detrusor repair caused slight improvement in 1 and then complete relapse, a maintained improvement but also slight difficulty in micturition in another, and very little advantage in the third.

Summary

The technique, complications and results of an anterior detrusor tube repair for urinary incontinence in children is described. It appears that this procedure is appropriate only for selected cases of urinary incontinence but that it is an operation which should be within the paediatric urologist's repertoire. It is simple to perform, but care should be taken, by omental packing, to prevent a sharp posterior lip to the newly formed bladder neck.

References

Dees, J. E. (1949). Congenital epispadias with incontinence. *Journal of Urology*, **62**, 513-522.

Flocks, R. H. and Culp, D. A. (1953). A modification of technique for anastomosing membranous urethra and bladder neck following total prostatectomy. *Journal of Urology*, **69**, 411-415.

Leadbetter, G. W. (1964). Surgical correction of total urinary incontinence. *Journal of Urology*, **91**, 261-266.

Michener, F. R., Thompson, I. M. and Ross, G. (1964). Urethrovesical tubularization for urinary incontinence. *Journal of Urology*, **92**, 203-205.

Tanagho, E. A., Smith, D. R., Meyers, F. H. and Fisher, R. (1969). Mechanism of urinary continence. II. Technique for surgical correction of incontinence. *Journal of Urology*, **101**, 305-313.

Young, H. H. (1908). Suture of the urethra and vesical sphincters for the cure of incontinence of urine. *Transactions of the Southern Surgical and Gynecological Association*, **20**, 210-217.

The Authors

D. Innes Williams, MD, MChir, FRCS, Consultant Urologist.
Howard Snyder, MD, Visiting Fellow.

British Journal of Urology (1976), **48**, 675-680 ©

A Simple Artificial Implantable Sphincter

MICHAEL ROSEN
Department of Urology, Wollongong Hospital, N.S.W., Australia

A new device to aid in the control of urinary incontinence is described. The idea of urethral compression to attain continence is not new (Berry, 1961; Kaufman, 1973; Scott, Bradley and Timm, 1974), but this device is physiologically superior because the urethra can be occluded and opened at will, in a simple fashion.

The Artificial Sphincter

The device is composed of a 3-pronged clamp, 2 arms of which are parallel on 1 side and a single arm carrying a balloon opposing them. These arms fit transversely across the urethra. The balloon is connected via reinforced tubing to a reservoir bulb containing isotonic saline and a release valve. The tubing is in 2 parts joined by a small connector piece to enable the device to be filled with isotonic saline. Compression of the bulb inflates the balloon elevating and compressing the urethra thus obtaining urethral compression and continence (Fig. 1). Voiding is performed on deflating the balloon by pressing the release valve. The reservoir bulb and valve is sited in the scrotum and is easily palpable and manipulated (Fig. 2). The whole device is constructed of medical grade silicone elastomer (Fig. 3).

The Patients

16 patients are presented. The period of incontinence varied from 8 months following an abdomino-perineal resection, to 19 years following trauma and consequent paraplegia. There were 6 cases of incontinence following a T.U.R. and 3 cases following an open prostatectomy, and in 1 case the patient had had 3 T.U.R.s followed by subsequent open prostatectomy. 3 cases followed abdomino-perineal resection, and 2 cases were neurogenic bladders (see Table).

All patients had a routine medical assessment and all had an I.V.P., cystoscopy and a micturating cystogram; some of the patients, in particular those with neurogenic disorders, had a cystometrogram. The operations were carried out under epidural anaesthesia in the majority of cases. Most patients received large doses of intravenous antibiotics commencing some hours before surgery and this was maintained for 48 hours and then oral antibiotics were continued for at least a week.

Method

The patients were prepared with shaving and cleansing of the skin of the lower abdomen, genitalia, perineum and buttocks on the evening before the operation. The bowel was sterilised with sulphathalazole for 3 days before the operation and neomycin the day before operation.

At operation the patient is placed in a slightly exaggerated lithotomy position and a 20 French

Read at the 32nd Annual Meeting of the British Association of Urological Surgeons in London, June 1976.

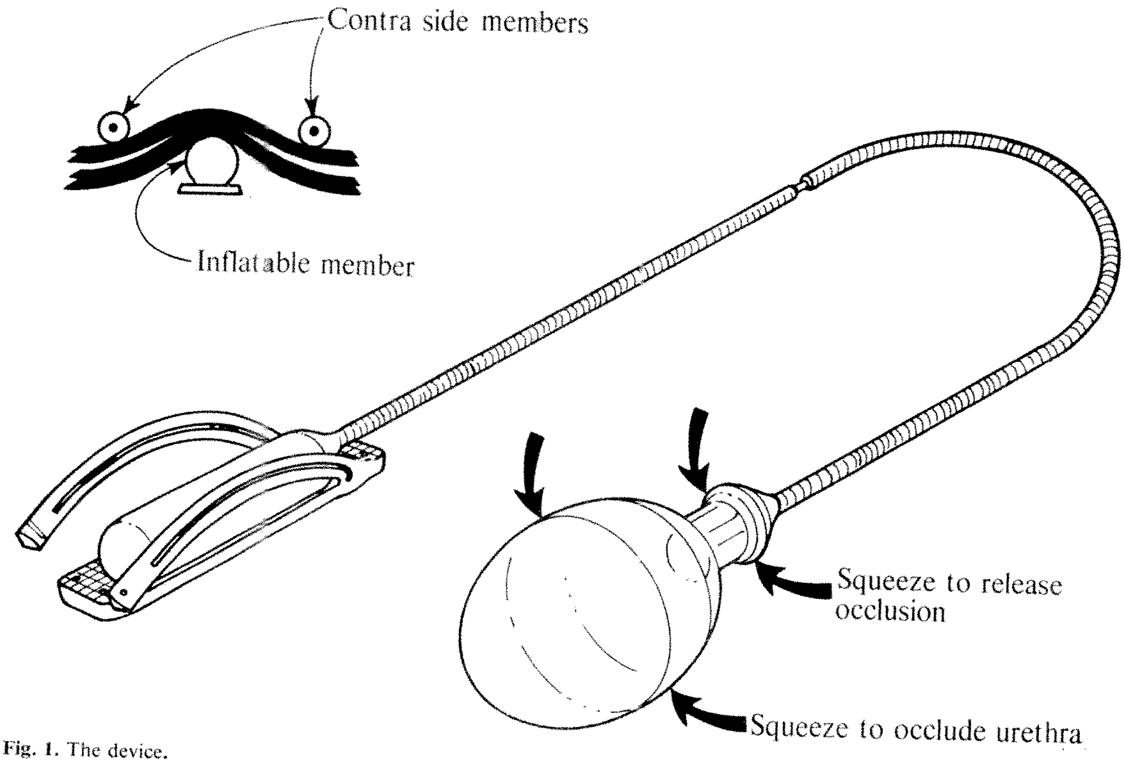


Fig. 1. The device.

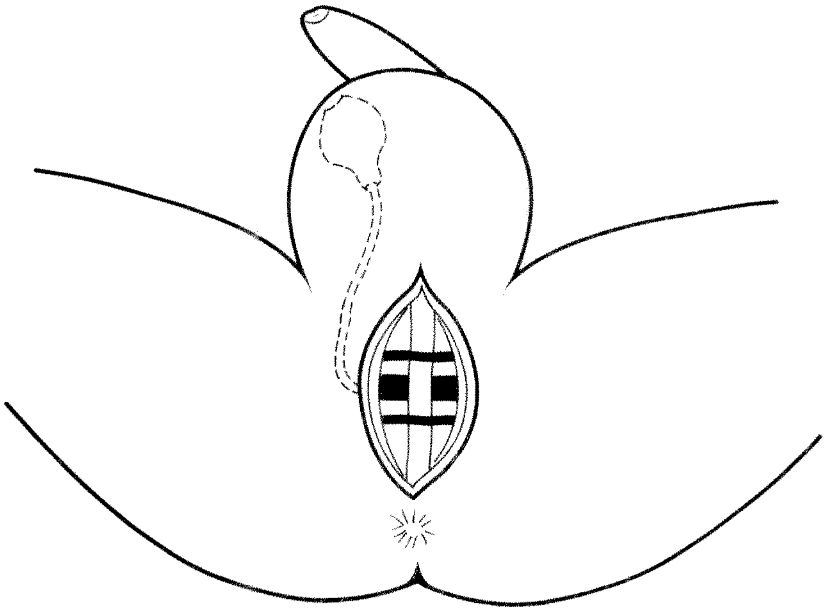


Fig. 2. The device *in situ*.

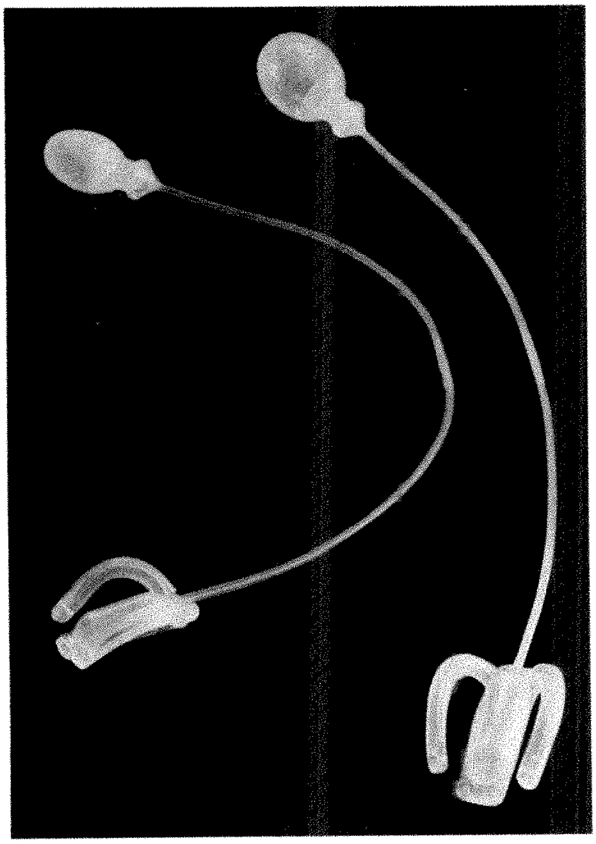


Fig. 3. Large and small device inflated.

sound is inserted in the urethra. An assistant's hand is used to steady the sound and push it forward into the perineum. The anus is covered by a "Steri-drape".

A midline perineal incision is made extending from the base of the scrotum to a point a little in front of the anus. The subcutaneous tissue is sharply incised in the midline until the perineal fascia and the urethral bulb is exposed. The urethra is then mobilised anteriorly and laterally from the fascia and deeply from the urogenital diaphragm. Superficial branches of the pudendal nerves and arteries on either side of the midline are not damaged by keeping in the midline. The urethra is separated from the urogenital diaphragm for a length of 2·5 cm. A ring retractor facilitates exposure. The sterilised prosthesis is filled to the maximum with isotonic saline. The 3-pronged clamp is then placed transversely across the urethra, the single arm deep and the parallel arms superficial. The sound is then removed. The parallel arms are then bent manually or with haemostats until they hold the urethra snugly. These arms are quite malleable and this manoeuvre is easily performed. The ends of the 3 arms are loosely approximated with a non-absorbable monofilament suture and then anchored to the urogenital diaphragm and deep surface of the perineal fascia. The arms on the other side of the urethra are similarly fixed. The tubing of the 3-pronged clamp is brought out by a stab wound through the perineal fascia laterally. At this stage the device is assembled and the tubing tied to the connector piece with non-absorbable sutures as a safeguard. The perineal fascia is sutured in the midline with a running continuous suture of 00 atraumatic catgut. Dissection is commenced to place the bulb in the scrotum and this is carried out in a superficial plane. The bulb having been placed in the scrotum the superficial perineal fascia is closed with a similar suture. The skin is closed with a running subcuticular suture of synthetic monofilament suture (Prolene) and the wound sprayed with protective adhesive.

No catheter is inserted and the device is left in the open position. The perineum receives dry

Table

Name	Age	Cause of incontinence	Period of incontinence	Date of operation	Result	Follow-up	Action	Final result	Comment
A. S.	71	T.U.R.	1 year	6 June, 1974	Cured	–	–	Cured	–
R. N.	83	Open prostatectomy	5 years	25 July, 1974	Cured	–	–	Cured	–
R. J. H.	55	T.U.R.	1½ years	28 Aug, 1974	Failed	–	Removal of device	Failed	Sepsis
R. P.	63	T.U.R.	1 year	2 Sept, 1974	Cured	Device failed	Insert new device	Cured	–
C. H.	74	Abdomino-perineal	2 years	6 Sept, 1974	Cured	–	–	Cured	–
F. B.	66	Open prostatectomy	2 years	29 Oct, 1974	Improved	–	Readjust device	Cured	–
A. Y.	47	Neurogenic U.M.N.	19 years	27 March, 1975	Cured	Infection	Device removed	Failed	Sepsis
F. H.	71	Open prostatectomy	6 years	3 July, 1975	Cured	–	–	Cured	–
H. C.	67	T.U.R.	1½ years	4 Sept, 1975	Failed	–	Device removed	Failed	Sepsis fistula
R. H.	60	Abdomino-perineal	1 year	9 Sept, 1975	Failed	–	Device removed	Failed	Sepsis
J. G.	65	T.U.R. (3) Open prost.	3 years	13 Nov, 1975	Failed	–	Device removed	Failed	Sepsis fistula
N. W.	71	T.U.R.	2 years	4 Dec, 1975	Failed	–	Second device	Improved	–
W. N.	71	T.U.R.	5½ years	27 Nov, 1975	Cured	–	–	Cured	–
R. C.	34	Cauda equina	7 years	5 Feb, 1976	Cured	Device failed	Second device	Cured	–
J. M.	65	Abdomino-perineal	8 months	26 March, 1976	Cured	–	–	Cured	–
H. H.	74	Urethrotomy	6 years	9 April, 1976	Cured	–	–	Cured	–

heat for 20 minutes twice daily and the running subcuticular suture is removed on the 7th day. The patient is not encouraged to manipulate the bulb even in the absence of scrotal oedema until the 7th day when the sutures are removed. The patient usually manages to manipulate the bulb very rapidly and can go home on the 9th or 10th day.

Results (Table)

Of the 16 patients operated on for a variety of reasons for incontinence, 10 have been cured, 1 improved and 5 failed. "Cure" was defined as not leaking any urine at all and not requiring pads or collecting devices, "improved" was defined as a patient who previously required a collecting device and now could wear pads or if he was already wearing pads, the number of pads used in a day was significantly reduced, and "failure" was defined as no improvement. No patient was made worse by the procedure.

Discussion

Several points for discussion emerge from the results. The incidence of fistula formation is low. It might have been thought that with direct compression of the urethra there would have been subsequent urethral wall necrosis and fistula development. In fact, only 2 cases of fistula occurred and 1 of these was iatrogenic. This patient (J. G.), on the evening of having the device inserted, developed gross scrotal oedema, extravasation of urine and retention and it was obvious that he had sustained urethral damage during the procedure of insertion. He had had 3 T.U.R.s, 1 open prostatectomy and a Kaufman prosthesis which had subsequently to be removed because of sepsis. A suprapubic cystotomy was done and he managed to retain the device for 3 months. The fistula in fact closed but there was so much woody oedema around the device that it could not be manipulated. It was painful to the patient and was therefore removed.

The other case of fistula (H. C.) developed some weeks following the insertion of the device. At no time was he able to manipulate the device and this fistula was certainly caused by and associated with infection. The device in this case was removed.

The other failures were due to sepsis. This was not the florid type of sepsis and in fact did not show much oedema, but there was tenderness at all times at manipulating the device and when finally the device was removed it could be seen that around the reservoir bulb there was a thick walled capsule with a 1 ml or less of pus present.

The "improved" case (N. W.) was due to a 2nd operation. At the 1st operation the device to be inserted was perforated and an older device had to be used. The operation went well and the patient recovered promptly but the device did not produce any significant reduction in his incontinence. 2 months later a 2nd device was put in. This was extremely easy to do and it was obvious at this time that the device becomes surrounded in non-infective cases by a thin serous lining. There was no difficulty in putting the urethral portion across the urethra and there was no suggestion of impending urethral wall necrosis. However, the device managed only to improve this patient, converting him from using a collecting device to pads.

The 2 cases of device failure were easily rectified. In 1 case the patient forgot to deflate the balloon to void and voided past the balloon; he felt and heard a popping sound in his perineum and became incontinent immediately. At reoperation a new device was inserted and this was successful. In the 2nd case of device failure, the connector piece had eroded through the reinforced tubing. In this case the 2 ends were freshened and a new connector piece inserted and this restored continence.

It can be seen from these results that most of the complications are due to infection and one cannot be too scrupulous about the preparation of the patient and the use of large doses of broad spectrum antibiotics intravenously at least initially. Epidural anaesthesia makes the operation very much easier, and age is no bar to surgery. The only contra-indications to this procedure would be in those patients afflicted with a gross intention tremor, Parkinson's disease or senility.

Summary

A device is presented for the cure of urinary incontinence in males.

16 cases have been operated on, 10 have been cured, 1 improved and 5 failed. Most of the failures were due to sepsis.

Despite this small number of cases the results are extremely encouraging.

The device, because of its simplicity, both in construction and ease of insertion, is considered worthy of extensive trials.

Addendum

Since this paper was delivered, 4 more cases of post-prostatectomy incontinence have been operated on and all have been cured.

References

BERRY, J. L. (1961). A new procedure for correction of urinary incontinence: preliminary report. *Journal of Urology*, **85**, 771-775.

KAUFMAN, J. J. (1973). Treatment of post-prostatectomy urinary incontinence using a silicone gel prosthesis. *British Journal of Urology*, **45**, 646-653.

SCOTT, F. B., BRADLEY, W. B. and TIMM, G. W. (1974). Treatment of urinary incontinence by an implantable prosthetic urinary sphincter. *Journal of Urology*, **112**, 75-80.

The Author

Michael Rosen, FRCS, Honorary Urologist.

British Journal of Urology (1976), **48**, 681-684 ©

Excretion Urography in the Investigation of Prostatism

P. H. ABRAMS, J. ROYLANCE and R. C. L. FENELEY
Departments of Urology and Radiodiagnosis, Bristol

The symptoms of frequency, nocturia, urgency, deterioration in stream, post-micturition dribble and hesitancy are frequently referred to as prostatism. This symptom complex has been associated with the presence of bladder outflow obstruction (Bailey and Love, 1971).

When such patients are investigated by excretion urography, the findings of trabeculation, diverticula, bladder wall thickness, basal prostatic filling defect and residual urine have been equated with bladder outflow obstruction (Shanks and Kerley, 1958; Sutton, 1969; Emmett and Witten, 1971).

In recent years urodynamic studies have become a recognised method of assessing lower urinary tract function (Bates and Corney, 1971; Turner Warwick *et al.*, 1973; Torrens *et al.*, 1976).

A consecutive series of 201 male patients presenting with prostatism have been studied by excretion urography and urodynamic studies to assess the significance of these radiological signs.

Patients

This series consists of patients presenting to hospital in the Avon Clinical Area with uncomplicated prostatism over a period of 15 months. Their ages ranged between 48 and 84. Those patients with acute retention of urine, chronic retention leading to urgent admission, renal failure or with other significant urological disease have been excluded.

Methods

The excretion urograms were reviewed without the knowledge of the patients' urodynamic findings. The area of the basal prostatic filling defect and the areas of the bladder on the preliminary, full and post-evacuation films were measured by planimetry. Bladder wall thickness was defined as the mean of 3 measurements taken between the outer contrast layer and the inner perivesical fat layer. Trabeculation on the full film was graded 0-3 against film standards selected at the beginning of the study.

The basic urodynamics measurement of rectal pressure (PA) total bladder pressure (PB), intrinsic bladder pressure (PI = PB − PA by electronic subtraction) and urine flow rate (F) were recorded.

Elema Schonander pressure transducers (EMT 34), a uroflow transducer (EMT 435) and a Mingograf M81 multichannel recorder were used for these recordings. The bladder was filled at 50 ml/min (temp 37°C) through an 8F catheter and the bladder pressure measured using an epidural catheter. When the bladder was full the filling catheter was removed leaving the epidural *in situ* during voiding.

The peak flow pressure and the peak flow rate were used to calculate the urethral resistance

Read at the 32nd Annual Meeting of the British Association of Urological Surgeons in London, June 1976.

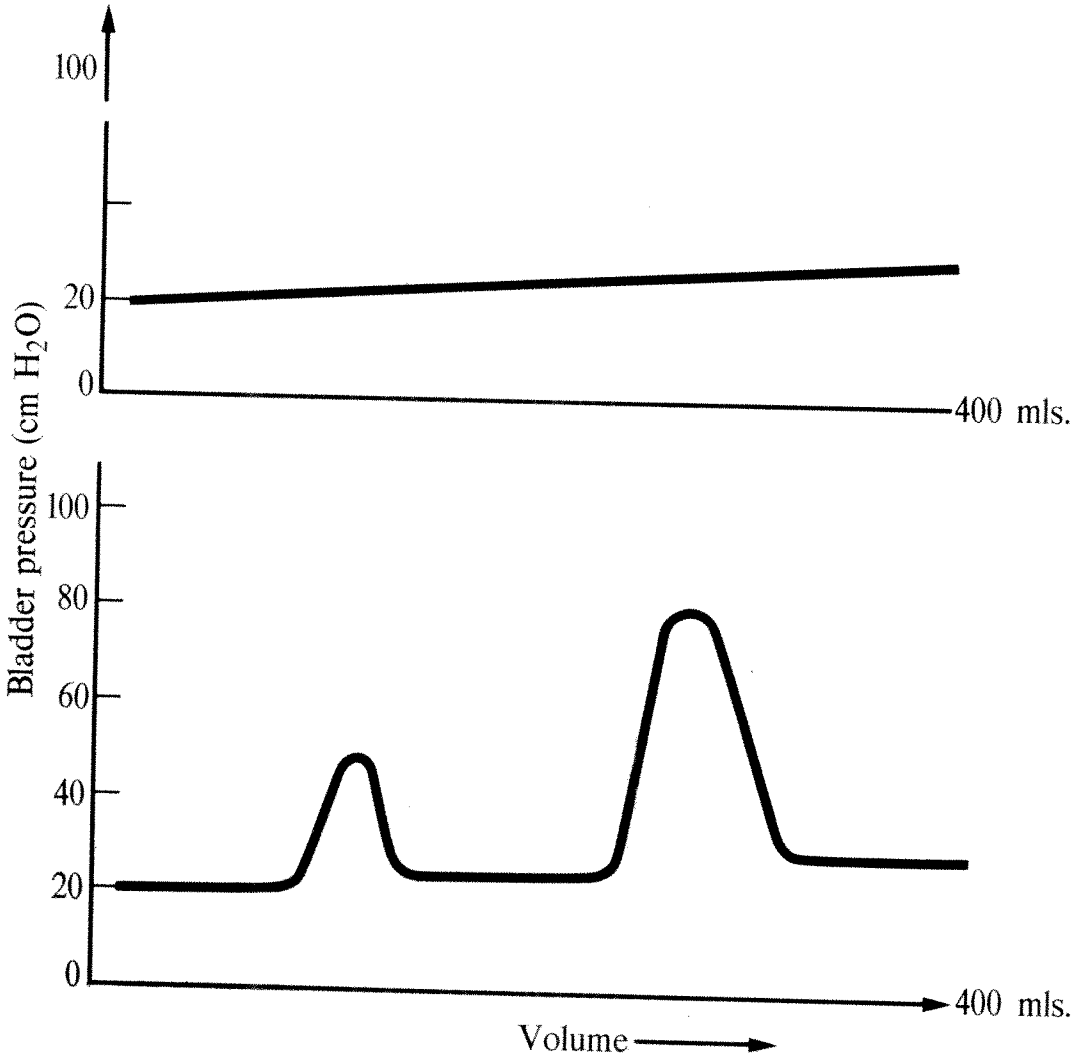


Fig. 1. Inflow cystometrograms: upper trace, normal; lower trace, unstable bladder.

factor from the formula pressure divided by the square of flow rate (Claridge, 1964; Smith, 1964).

Results

Complete urodynamic data were obtained on 199 patients. 1 patient could not micturate and 1 patient could not be catheterised. A group of 5 patients had underactive detrusor muscles on micturition and have not been included in the analysis. The inflow cystometry demonstrated unstable waves of bladder activity in 56% of patients (Fig. 1). Pressure-flow analysis of micturition

Table I

Patient Groups Defined by Urodynamic Studies

Total (194 patients)	Stable bladder (85 patients)	Unstable bladder (109 patients)
Normal micturition (61 patients)	35 (18%)	26 (13%)
Obstructed micturition (133 patients)	50 (26%)	83 (43%)

showed that 133 patients (60%) had obstructed micturition defined as a urethral resistance factor greater than 0·6. The patients thus fall into 4 main groups (Table I).

Trabeculation was seen in 65% of patients and was found to be significantly related to bladder instability ($P < 0\cdot025$) but not to outflow obstruction ($P < 0\cdot2$) although instability was found to be associated with obstruction ($P < 0\cdot01$). Similar significance levels were obtained by using log linear models in contingency tables. Diverticula were shown in 12 patients (6%) and were similarly associated with instability ($P < 0\cdot02$), but not with obstruction ($P = 0\cdot7$).

The bladder area of the full film and bladder wall thickness were not shown to have any significant associations ($P = 0\cdot2$).

The basal prostatic filling defect (range 0-34 sq. cm) was associated with obstruction and the larger the defect the greater the incidence of associated obstruction ($P < 0\cdot001$). Prostatic calculi were seen in 29% of patients but their presence was not related to either prostatic size or obstruction.

The preliminary bladder shadow and the bladder area on the void film were similar on 87% of occasions when both could be visualised. When these areas were compatible there was a close association with obstruction ($P < 0\cdot01$) and the measured residual urine ($P < 0\cdot001$).

10 patients (5%) had upper tract dilatation which was unilateral in 3 cases. Dilatation was associated with moderate and severe trabeculation ($P < 0\cdot001$) although not with outflow obstruction ($P = 0\cdot2$) or with instability ($P = 0\cdot2$).

14 patients (7%) had co-existing upper tract pathology: renal cyst (6), renal calculi (2), pyelonephritic kidneys (2), congenitally malrotated kidneys (2), horseshoe kidney (1) and absent kidney (1). 3 patients (1·5%) had bladder calculi.

Discussion

The results of this series suggest that more than half of patients presenting with prostatism have an unstable bladder which contracts intermittently during filling. The aetiology of this condition has not yet been fully explained. Instability has been shown to occur in all age groups and to be associated with the symptoms of frequency, nocturia, urgency, urge incontinence and enuresis (Turner Warwick *et al.*, 1973; Dunn, Smith and Ardran, 1974; Torrens *et al.*, 1976). This series also suggests that two-thirds of patients with prostatism have outflow obstruction and that more than half of those obstructed have an associated unstable bladder. Instability has also been shown to occur in the absence of obstruction and it may be this group of patients that has given rise to the cautionary advice in considering prostatectomy for frequency and urgency (Mitchell, 1972).

The value of excretion urography in this group might include the demonstration of upper tract abnormalities. However, such abnormalities were infrequent and did not alter patient management. Similar conclusions were reached following the investigation of patients with acute retention (Marshall, Singh and Blandy, 1975). Demonstration of trabeculation and diverticula will suggest the presence of bladder instability. A basal prostatic impression and evidence of residual urine suggest the presence of outflow obstruction. Before the diagnosis of residual urine is made it is important to confirm that the bladder shadow on the preliminary film is comparable to that on the post-micturition film. Then the area of the bladder corresponds quite accurately with the actual volume of residual urine (Griffiths and Castro, 1970).

This study has demonstrated associations between some of the features of excretion urography and urodynamic studies but has not defined the exact position or relevance of either investigation to the management of patients with prostatism. By continuing to perform both investigations and the long-term follow-up of those patients already investigated it is hoped that a clearer picture will emerge.

Summary

The excretion urogram and urodynamic studies of 201 patients presenting with prostatism were reviewed.

The urographic features of trabeculation and diverticula were found to be associated with bladder instability as shown on inflow cystometry but not to be associated with outflow obstruction as shown by the pressure-flow analysis of micturition.

The bladder shadow on the preliminary film, and the bladder size on the post-evacuation film were associated with the measured residual urine and with outflow obstruction.

The basal prostatic filling defect was also associated with outflow obstruction.

We are grateful to the urologists of the Avon Clinical Area for allowing us to investigate patients under their care, and to the Medical Research Council for financial support (Project Grant G974/135C). Our thanks also go to Mrs S. Price for typing this manuscript, and to Mrs Audrey Morris of Community Health, and Dr Susan Evans of the Computer Unit, Bristol University for their help in data processing and statistical analysis.

References

Bailey, H. and Love, M. (1971). *Short Practice of Surgery*, 15th ed. London: Lewis, p. 1182-1188.

Bates, C. P. and Corney, C. E. (1971). Synchronous cine/pressure/flow cystography: a method of routine urodynamic investigation. *British Journal of Radiology*, **44**, 44-50.

Claridge, M. (1964). "Hydrodynamics of micturition." Ch.M. Thesis, University of Oxford.

Dunn, M., Smith, J. C., and Ardran, G. M. (1974). Prolonged bladder distension as a treatment of urgency and urge incontinence of urine. *British Journal of Urology*, **46**, 645-652.

Emmett, J. L. and Witten, D. M. (1971). Obstruction of the bladder outlet in adult men: benign prostatic hyperplasia. *Clinical Urography*, 3rd ed. Philadelphia: Saunders, **1**, 562-575.

Griffiths, H. J. L. and Castro, J. (1970). An evaluation of the importance of residual urine. *British Journal of Radiology*, **43**, 409-413.

Marshall, V., Singh, M., Blandy, J. P. (1975). Is urography necessary for patients with acute retention of urine before prostatectomy? *British Journal of Urology*, **47**, 73-76.

Mitchell, J. P. (1972). *The Principles of Transurethral Resection and Haemostasis*. Bristol: Wright.

Shanks, S. C. and Kerley, P. (1958). *A Textbook of X-ray Diagnosis*, 3rd ed., Vol. 3. London: Lewis, p. 850.

Smith, J. C. (1964). Some theoretical aspects of urethral resistance. *Investigative Urography*, **1**, 477-481.

Sutton, D. (1969). *Textbook of Radiology*. Edinburgh: Livingstone, p. 802.

Torrens, M. J., Abrams, P. H., Dunn, M., Collings, C. D., Tribe, B., Lewis, P. and Feneley, R. C. L. (1976). The definition and clinical associations of the hyperactive bladder. *Urologia Internationalis* (in press).

Turner Warwick, R., Whiteside, C. G., Arnold, E. P., Bates, C. P., Worth, P. H. L., Milroy, E. G. J., Webster, J. R. and Weir, J. (1973). A urodynamic view of prostatic obstruction and the results of prostatectomy. *British Journal of Urology*, **45**, 631-645.

The Authors

P. H. Abrams, FRCS, Research Registrar.
J. Roylance, DMRD, FRCR, Consultant Radiologist.
R. C. L. Feneley, MChir, FRCS, Consultant Urologist.

British Journal of Urology (1976), **48**, 685-687 ©

Hypothermic Prostatic Resection

A. SERRAO, M. K. MALLIK, P. A. JONES, W. F. HENDRY and J. E. A. WICKHAM
Department of Urology, St Bartholomew's Hospital, London EC1

Many attempts have been made to find agents which will reduce bleeding in prostatic surgery and allow the performance of a more accurate and better visualised operative procedure.

Various clotting agents have been used to achieve this result but none is completely free of risk mainly because of the high incidence of degenerative cardiovascular disease in patients of this age-group. This objection does not apply to substances which inhibit fibrinolysis such as epsilon amino caproic acid (EACA). Vinnicombe and Shuttleworth (1966*a*) showed that EACA 0·5 g 4-hourly for 12 hours reduced post-prostatectomy blood loss to one-third of that of untreated controls and, equally important, that the drug was therapeutically safe with no apparent side-effects (Vinnicombe and Shuttleworth, 1966*b*).

Another means used to achieve reduction in blood loss has been the use of localised hypothermia to the bladder or prostatic area.

The principal physiological responses to hypothermia are:

1. Lowered cell metabolism.
2. Increased blood viscosity.
3. Vasoconstriction.

The vasoconstriction and increased blood viscosity induced by cold have been used clinically to control bleeding from peptic ulcers (Wangensteen *et al.*, 1959) where they have been shown to reduce blood flow in the stomach by 66%.

It seemed that, in a situation where reduced blood flow would be an obvious advantage, it was illogical to perfuse the organ with a warm irrigant and that a low temperature perfusate might have considerable benefits.

This same thought had attracted others in the past: thus Landes *et al.* (1959), reported decreased blood loss during T.U.R. by the use of cooled irrigant. The loss was not quantified but its reduction was judged to be "so marked as to be unquestionable". Postoperative bleeding was also reported as being reduced.

Cockett, Schultz and Franks (1961), however, found no appreciable reduction in blood loss during T.U.R. with cooled irrigant, whereas Robson and Sales (1966) reported the technique to be beneficial. In the latter studies only the per-operative blood loss was measured.

In view of these conflicting reports, we felt that a statistically valid quantitative comparison of blood loss during T.U.R. should be made using conventional irrigant at 37°C and cooled irrigant at 2°C. It was also decided to estimate postoperative blood loss over the 3 days after T.U.R.

Method and Patients

20 patients were chosen and divided into 2 groups: 1 was taken as a control and underwent T.U.R. using a body temperature irrigating solution, and the second underwent T.U.R. with

Read at the 32nd Annual Meeting of the British Association of Urological Surgeons in London, June 1976.

Table I

Comparison of Excised Gland Weights, Operative Times, Volume of Irrigant used and Operative Blood loss in Control (Warm) and Cold T.U.R. Groups (Mean ± standard error)

	Gland weight (g)	Operating time (min.)	Irrigant volume (ml)	Blood loss (G Hb)
Control (Warm) T.U.R.	8·2 ± 1·4	35·2 ± 2·8	7287 ± 702	20·9 ± 2·6
Cold T.U.R.	7·1 ± 0·7	25·3 ± 5·5	4628 ± 48·7	3·4 ± 0·8
Statistical significance (Student's *t* test)	N.S.	N.S.	P < 0·002	P < 0·001

Table II

Comparison of Blood Loss in grams of haemoglobin on the First 3 Postoperative Days in Control (Warm) and Cold T.U.R. Groups. (Mean ± standard error)

	Postoperative day 1	2	3	Total
Control (Warm) T.U.R.	14·3 ± 6·0	5·7 ± 2·5	2·8 ± 1·1	22·8 ± 9·5
Cold T.U.R.	7·0 ± 3·8	2·6 ± 0·9	2·3 ± 0·7	12·7 ± 5·6
Statistical significance (Student's *t* test)	N.S. 0·5 > P > 0·2	N.S. 0·5 > P > 0·2	N.S. P > 0·5	N.S. 0·5 > P > 0·2

irrigant cooled to 2°C. Excluded from the selection were those patients who had had previous operations on the prostate, those suffering from carcinoma of the prostate and those with blood dyscrasias.

The patients were taken randomly from the waiting list, although those patients with an estimated gland size of over 30 g were excluded. A standard anaesthesia was adopted and the same type of resectoscope was used in all operations. One variable which may vitiate any evaluation of blood loss during T.U.R. is the ability of the surgeon. In this study, however, the operations were carried out by 2 surgeons who were considered competent at transurethral prostatic resection.

At the end of each operation the irrigating fluid was collected, the volume measured and a well-mixed representative sample was sent for haemoglobin estimation. The group to which the patient belonged was not disclosed to the haematologist. The blood loss was measured by a colorimetric determination on an aliquot of irrigating fluid. This method has been used by other investigators (Durante *et al.*, 1962; Perkins and Miller, 1969) and has been found to be accurate and reproducible, the margin of error in the evaluation being less than 6%. We judge this to be more accurate than the Sahli acid haematin determination (as described by Gatch and Little, 1924) and the radioactive method (Cockett *et al.*, 1961).

Estimations were made on 1 operative specimen and 3 daily postoperative samples from complete 24-hour urine collections. The excised gland chippings were weighed.

Results

The results of this study are presented in Tables I and II.

In Table I the excised gland weights are compared between the 2 groups and no statistical difference is found. The mean of operation times shows that the cold group took 10 minutes less time to complete the operation but this is not statistically significant. The amount of irrigant used in the cold group was however, significantly less and the haemoglobin loss at operation was dramatically less in the cold group with only 3·4 g of haemoglobin being lost compared with 20·9 g, a 6-fold reduction.

In Table II the blood loss on the 3 successive postoperative days is shown. Although the total is less in the cooled group and is nearly half that found for the controls, the differences are not statistically significant.

Discussion

There is thus unequivocal evidence in this series that blood loss during T.U.R. can be dramatically reduced by the very simple measure of using a cooled irrigant solution. Per-operative blood loss is reduced almost 6-fold and, as might be expected, postoperative blood loss is not so much influenced by this procedure, the most beneficial effects of the hypothermia being restricted to the period of time when the cooling process is exerting its vasoconstrictive and "viscostatic" effect.

Certainly the statistical evaluation strongly supports our subjective impression that blood loss can be significantly reduced per-operatively by this simple procedure. We would commend the use of cooled glycine to all transurethral resectors.

The advantages of reduced haemorrhage in the elderly requires no elaboration.

Summary

A simple method of markedly reducing blood loss during T.U.R. is reported.

Cooling of the irrigant solution to 2°C by placing the glycine in a domestic refrigerator reduces the operative blood loss 6-fold.

References

Cockett, A. T. K., Schultz, J. and Franks, D. (1961). Use of refrigerated solutions during transurethral surgery. *Journal of Urology*, **85**, 632-635.

Durante, L. J., Moutsos, A., Ambrose, R. B., Duncan, W. Y., Fleming, W., Zinsser, H. H. and Phillips, L. L. (1962). Post prostatectomy bleeding. *Annals of Surgery*, **156**, 781-792.

Gatch, W. D. and Little, W. D. (1924). Amount of blood lost during some of the more common operations. *Journal of the American Medical Association*, **83**, 1075-1076.

Landes, R. R., Leonhardt, K., Ransom, C. L. and Davila, J. (1959). Localized hypothermia for transurethral prostatic resection. *Journal of Urology*, **82**, 247-248.

Perkins, J. B. and Miller, H. C. (1969). Blood loss during transurethral prostatectomy. *Journal of Urology*, **101**, 93-97.

Robson, C. J. and Sales, J. L. (1966). The effect of local hypothermia on blood loss during transurethral resection of the prostate. *Journal of Urology*, **95**, 393-395.

Vinnicombe, J. and Shuttleworth, K. E. D. (1966*a*). Aminocaproic acid in the control of haemorrhage after prostatectomy. A controlled trial. *Lancet*, **1**, 230-231.

Vinnicombe, J. and Shuttleworth, K. E. D. (1966*b*). Aminocaproic acid in the control of haemorrhage after prostatectomy. Safety of aminocaproic acid—a controlled trial. *Lancet*, **1**, 232-234.

Wangensteen, O. H., Salmon, P. A., Griffen, W. O., Paterson, J. R. S. and Fattah, F. (1959). Studies of local gastric cooling as related to peptic ulcer. *Annals of Surgery*, **150**, 346-358.

The Authors

A. Serrao, MCh, Urological Registrar.
M. K. Mallik, FRCS, Urological Registrar.
P. A. Jones, FRCS. (At present, Surgical Registrar, Royal West Sussex Hospital, Chichester.)
W. F. Hendry, ChM, FRCS, Consultant Urologist.
J. E. A. Wickham, MS, BSc, FRCS, Senior Consultant Urologist.

British Journal of Urology (1976), **48**, 689-696 ©

Lymphography and Pelvic Lymphadenectomy in Carcinoma of the Prostate

E. P. N. O'DONOGHUE, P. SHRIDHAR, T. SHERWOOD, J. P. WILLIAMS and G. D. CHISHOLM
Institute of Urology and St Peter's Hospitals, Hammersmith Hospital and Greenwich District Hospital, London

The significance of lymph node metastases in prostatic carcinoma is not in dispute. Flocks (1973) has shown that the 15-year survival rate for Stage C disease treated by a combination of surgery, interstitial irradiation and hormonal therapy was 27·5% when the regional nodes were free of metastases, but only 12·5% in the presence of nodal deposits. Other studies have shown that nodal spread frequently precedes and is probably unrelated to skeletal metastases (Zingg *et al.*, 1974; Paxton, Williams and Macdonald, 1975). The most widely used staging system, first described by Whitmore (1956) does not permit the ready classification of nodal spread. The application of the TNM system to the prostate was recommended by the International Union against Cancer (U.I.C.C.) in 1967 and a recent revision is now in use (Wallace, Chisholm and Hendry, 1975). The minimal requirements for the N-category consist of clinical examination, lymphography and/or urography. However, the accuracy of lymphography in the detection of nodal metastases continues to be a source of some controversy in many tumour sites. The principal

Table I

TNM Classification in 45 Patients with Carcinoma of the Prostate

- 45
  - 18 M1 NX
    - 1 T0
    - 2 T2
    - 11 T3
    - 4 T4
  - 27 M0 NX
    - 7 M0 NX
      - 3 T2
      - 3 T3
      - 1 T4
    - 20 Lymphography / Lymphadenectomy
      - 6 M0 N+ ... 6 T3
        - [N0 4, N2 1, N4 1]
      - 14 M0 N− ...
        - 1 T1
        - 7 T2
        - 6 T3
        - [N0 13, N2 1]

Read at the 32nd Annual Meeting of the British Association of Urological Surgeons in London, June 1976.

Table II

Results of Lymphography and Lymphadenectomy

	Lymphogram	
	+	−
20 Patients	3	17
Lymphadenectomy +	2	④
Lymphadenectomy −	①	13
		False negative 24%

Table III

Lymphadenectomy; Sampling Rates and Incidence of Metastases in Pelvic Lymph Nodes

Lymph nodes	Sampling rate	Incidence of metastases
External iliac	39/40	10/39
Common iliac	39/40	8/39
Internal iliac	27/40	9/27
Obturator	8/40	2/8

aims of this study were to assess the accuracy of lymphographic interpretation and the feasibility of pelvic lymphadenectomy in staging prostatic carcinoma.

Patients and Methods

A consecutive series of 45 new patients with histologically confirmed carcinoma of the prostate, has been categorised according to the TNM classification. The T-category was obtained from rectal and cystoscopic examination prior to treatment. The M-category was assessed in all patients and was based mainly on the results of bone scanning (^{99m}Tc-Sn-EHDP) and skeletal survey (Shearer *et al.*, 1974; Buck *et al.*, 1975). 18 of the 45 patients had evidence of skeletal deposits (*i.e.* M1). It is our opinion that N categorisation of an M1 patient is unnecessary as metastatic disease has been demonstrated: thus the final designation of these patients is M1 NX. Of the remaining 27 patients, 7 were either too old (>75 years), too infirm or believed to have inadequate pulmonary reserve for lymphography (M0 NX). Thus 20 M0 patients were selected for N studies (Table I).

Pedal lymphography was performed by a standard technique with antero-posterior and oblique views in the filling phase and again 24 hours later in the storage phase. Follow-up examinations were made before and after lymphadenectomy. The lymphograms were interpreted and reported as a routine service by the Radiology Department and were subsequently critically reviewed without knowledge of the histological findings by a panel of radiologists and clinicians. The criteria adopted for the diagnosis of metastatic deposits were as follows:

1. Focal nodal filling defects greater than 5 mm in diameter.
2. Grossly disordered nodal filling patterns.
3. Total obliteration of nodes.
4. Obstructed lymph channels were regarded as supportive but not diagnostic evidence.

Pelvic lymphadenectomy was carried out under general anaesthesia by a retroperitoneal approach via bilateral Rutherford Morrison incisions. A minimum interval of 2 weeks was allowed to elapse between lymphography and surgery because of the risk of a temporary reduction of pulmonary reserve from oil embolism. In the early cases, random sampling of external, common and internal iliac/obturator nodes was performed. It was soon evident that this was insufficient for a proper comparison with lymphography. The external and common iliac chains were therefore dissected *en bloc* but sampling of the internal iliac and obturator groups was limited to readily identifiable nodes.

Results

The N-categories in 20 patients are summarised in Table II. 3 of the 20 patients were considered to have nodal metastases on lymphography. However, subsequent histological examination showed 1 of these to be a false positive interpretation. Of the 17 patients with negative lymphograms, 4 had histological evidence of nodal metastases. The overall accuracy of lymphography was therefore 75% and the false negative rate 24%. Examples of the problems of interpretation are shown in Figures 1-4.

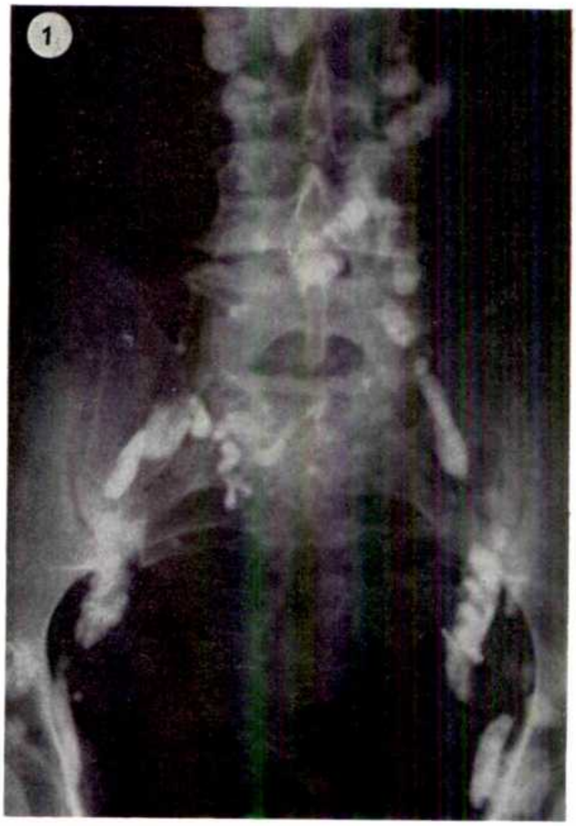
1 patient had unilateral lymphadenectomy because of anxiety regarding his cardiac state during anaesthesia. Representative nodes were thus obtained from 39 of 40 external and common iliac node groups (Table III). Sampling of the internal iliac and obturator groups was, however, much less complete, and only 27 of 40 and 8 of 40 respectively were obtained for histological study. The incidence of metastases for each of these groups is shown in the right-hand column of Table III. The relationship of nodal metastases to the side of the primary tumour is summarised in Table IV. There was no correlation between the side of the primary tumour and the site of nodal metastases.

Pelvic lymphadenectomy was a well-tolerated procedure with minimal morbidity, and no mortality. 1 patient suffered a small pulmonary embolism; a wound abscess, persisting for 10 days, and paralytic ileus for 5 to 6 days were single complications in individual patients. 5 patients

Table IV

Lymphadenectomy; Incidence of Nodal Metastases Related to Site of Primary

	L sided primary		R sided primary	
Lymph nodes	L nodes	R nodes	L nodes	R nodes
External iliac	2/7	2/7	4/13	2/12
Common iliac	1/7	2/7	3/13	2/12
Internal iliac	2/3	1/6	3/9	3/9
Obturator	1/2	1/1	0/2	0/3



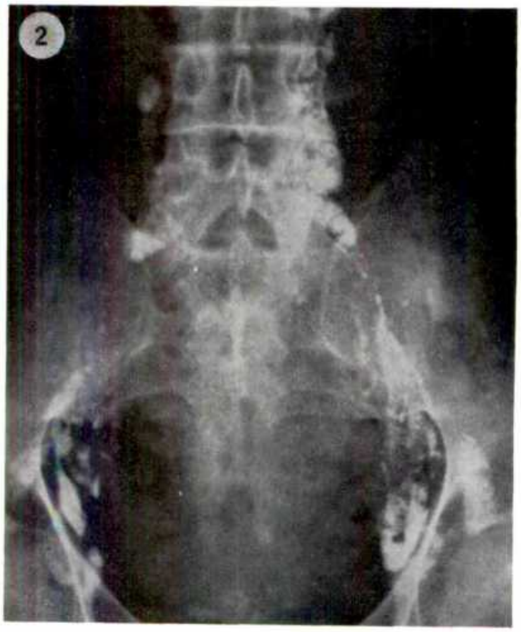


Fig. 1. In this representative film from an apparently normal lymphogram, none of the established criteria of metastases are present, but histological examination revealed multiple metastases.

Fig. 2. A more difficult problem of interpretation. There are multiple small filling defects in many nodes and a suggestion of obstructed lymphatic channels on the left. Nevertheless the accepted criteria are not present and this was judged a negative examination. Again multiple metastases were found on histological examination.

developed temporary genital oedema which resolved by the time of their discharge from hospital. The mean postoperative stay was 12 days.

The final TNM classification for the 45 patients is summarised in Table I. 6 of the 20 patients who underwent N studies had histologically proven nodal metastases and are therefore designated M0 N+ in the U.I.C.C. "shorthand". The clinical N category, based on lymphography, is shown in brackets and records the 4 false negative results as N0. All 6 patients with N+ disease had T3 tumours. Of the 14 patients with M0 N0 disease the T-category was T1 in 1, T2 in 7 and T3 in 6. The clinical N-category based on lymphography is shown in brackets, and the 1 false positive result recorded as N2. Of the 12 T3 M0 patients undergoing lymphography and lymphadenectomy exactly 50% had nodal metastases.

Discussion

The incorporation of lymphography and lymphadenectomy into a staging protocol for prostatic carcinoma may appear to be an excessive burden both to the patient and a clinical service. In the long term, it can only be justified by significantly improved results based on the rational

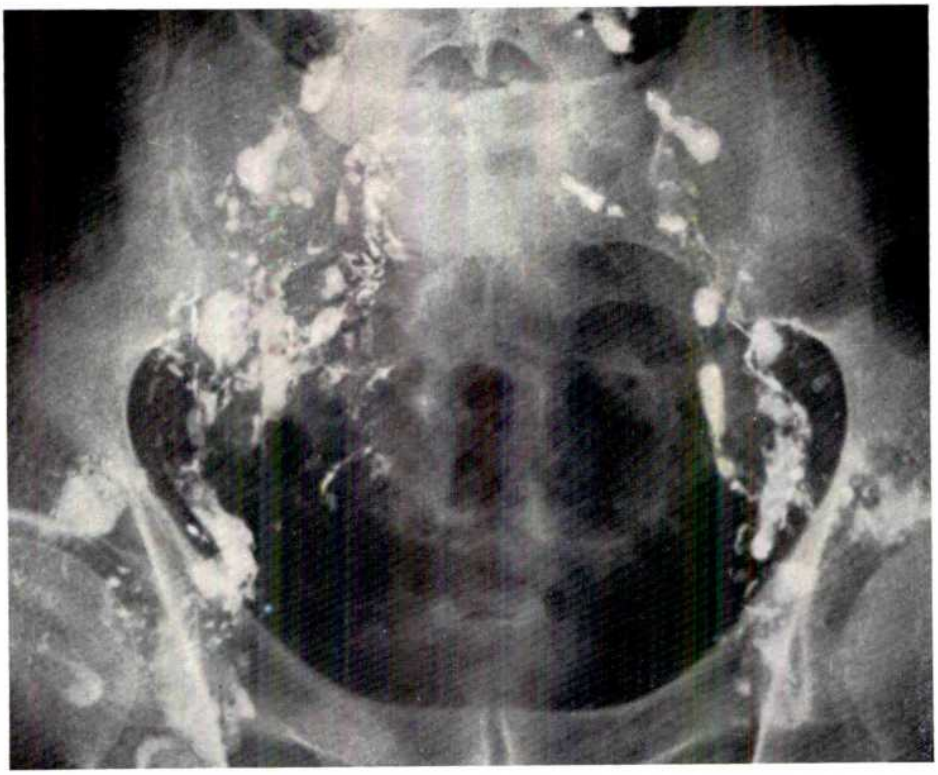


Fig. 3. There is evidence of obstructed and grossly disorganised lymphatic channels on the right but no evidence of nodal filling defects. By the strictest criteria this would be deemed a negative lymphogram although we judged it to be positive, which it was proved to be.

selection of appropriate treatment. It should be emphasised that not all patients require such a detailed assessment and the non-invasive techniques for the M category should precede consideration of the N category. In this series 20 of 45 patients underwent assessment of the N category (18 were M1 and 7 were too old or too infirm).

The problems of pedal lymphography in the staging of malignant disease in the pelvis are well known, especially concerning the accuracy of interpretation. In addition, the internal iliac and obturator node groups are not normally opacified. The overall accuracy rate in this series was 75% as assessed by histological examination. Accuracy rates of 89% (Castellino *et al.*, 1973) and 83% (Cerny *et al.*, 1975) are quoted in the literature in 2 other series. It may be relevant, however, that only selected patients underwent lymphadenectomy following lymphography in these 2 studies. Zingg *et al.* (1974) claimed that strict diagnostic criteria guaranteed an accuracy rate of 85 to 90% in their series and supported this assertion by reference to previous studies in Berne on carcinoma of the uterine cervix. In their prostatic series however, only 6 of 60 patients underwent lymphadenectomy; all 6 had negative lymphograms. In our own series all patients selected for N-categorisation have been prospectively studied by lymphography and lymphadenectomy. An accuracy rate of 75% would seem considerably less than ideal and the principal error is one of false negative interpretations. It may be argued that undetected microscopic deposits in regional nodes are not necessarily of significance in terms of survival and may be adequately treated by wide field pelvic irradiation. Flocks' (1973) data, however, would deny the first premise and such long-term studies as are available would indicate that survival is not

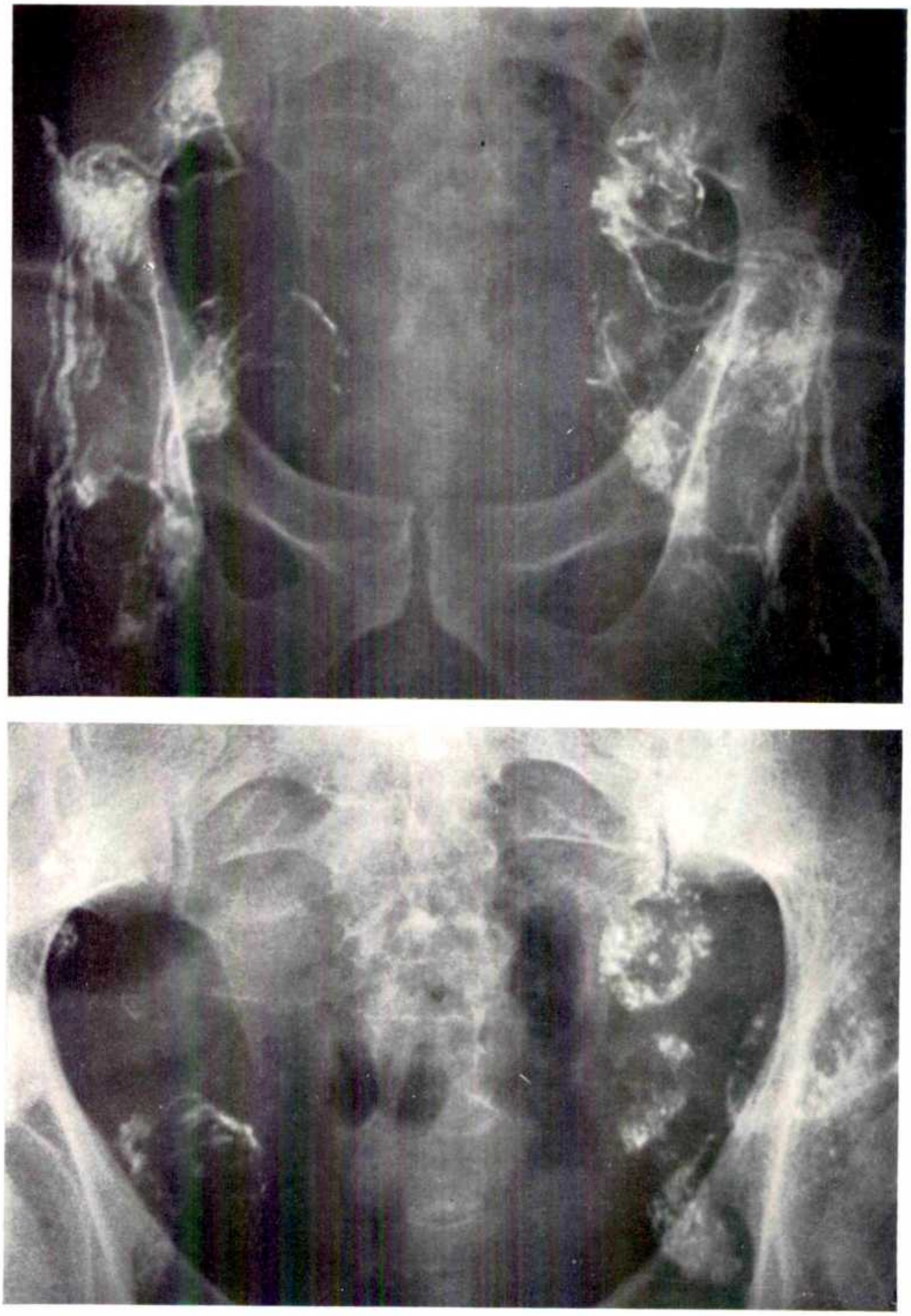


Fig. 4. An unequivocally positive lymphogram with grossly obstructed lymphatic channels on filling (A) and large nodal filling defects on the storage phase (B).

Table V

Incidence of Nodal Metastases in Carcinoma of the Prostate

	T0 M0	T1 M0	T2 M0	T3 M0	M1
	A	B_1	B_2	C	D
	(%)	(%)		(%)	(%)
Flocks *et al.* (1959)	–	7		38	–
Arduino and Glucksman (1962)	–	13		91	–
Whitmore *et al.* (1972)	–	25		55	–
Zingg *et al.* (1974)*	14	37		68	–
Collected series:					
McCullough *et al.* (1974)	–	21		40	–
Paxton *et al.* (1975)*	0	25	46	60	92
Rost *et al.* (1975)*	33	43		31	62
McLaughlin *et al.* (1976)	–	21	30	50	–
Nicholson *et al.* (1976)	–	8	14	33	–
Wilson *et al.* (1976)	–	14	45	53	–
O'Donoghue *et al.* (1976)	–	0	12	44	–

* Lymphography.

significantly different regardless of whether irradiation is applied to a small pelvic field (Ray, Cassady and Bagshaw, 1973) or to a large pelvic field (Hill, Crews and Walsh, 1974).

The reported incidence of lymph node metastases in prostatic carcinoma is summarised in Table V. There are difficulties in comparing the TNM system with the variations of Whitmore's staging system, but the information presented gives an indication of the reported incidence in the literature. Surprisingly 2 lymphographic series report a significant incidence of nodal metastases in T0 (Stage A) disease. In T1 and T2 the incidence is approximately 20% and recent reports support the distinction between T1 and T2 tumours. Of greater practical importance, 50% of T3 M0 tumours have not spread to lymph nodes.

McLaughlin *et al.* (1976) have shown that obturator-internal iliac nodes were the most frequently involved, and this must limit the value of pedal lymphography. Our low sampling rates of these nodes has indicated that dissection of the obturator fossa is preferable to "pluck" sampling. Although most of our N+ patients had bilateral nodal involvement, McLaughlin *et al.*'s (1976) figure was 57% and at present unilateral lymphadenectomy would seem insufficient.

Lymphadenectomy in this series was a reliable and safe procedure and provided accurate N-classification in 20 patients. Only 7 of 45 patients could not be adequately classified in terms of N and M. The remaining 38 were randomised to prospective therapeutic trials, based on the presence or absence of metastases (Chisholm and O'Donoghue, 1975).

Summary

20 of 45 new patients with prostatic carcinoma have undergone lymphography and lymphadenectomy to determine the N-category.

The overall accuracy of lymphography was 75%.

Lymphadenectomy was a safe procedure with minimal morbidity.

Although it would be premature to recommend its universal adoption in the management of this disease, its further application and study seems desirable.

Full TNM classification has proved to be of considerable value in the management of these patients.

This study confirms that 50% of T3 M0 tumours are free of lymph node metastases.

References

Arduino, L. J. and Glucksman, M. A. (1962). Lymph node metastases in early carcinoma of the prostate. *Journal of Urology*, **88**, 91-93.

Buck, A. C., Chisholm, G. D., Merrick, M. V. and Lavender, J. P. (1975). Serial fluorine-18 bone scans in the follow-up of carcinoma of the prostate. *British Journal of Urology*, **47**, 287-294.

Castellino, R. A., Ray, G., Blank, N., Govan, D. and Bagshaw, M. (1973). Lymphangiography in prostatic carcinoma. Preliminary observations. *Journal of the American Medical Association*, **223**, 877-881.

Cerny, J. C., Farah, R., Rian, R. and Weckstein, M. L. (1975). An evaluation of lymphangiography in staging carcinoma of the prostate. *Journal of Urology*, **113**, 367-370.

Chisholm, G. D. and O'Donoghue, E. P. N. (1975). The non-surgical treatment of prostatic carcinoma. *Vitamins and Hormones*, **33**, 377-397.

Flocks, R. H., Culp, D. and Porto, R. (1959). Lymphatic spread from prostatic cancer. *Journal of Urology*, **81**, 194-196.

Flocks, R. H. (1973). The treatment of Stage C prostatic cancer with special reference to combined surgical and radiation therapy. *Journal of Urology*, **109**, 461-463.

Hill, D. R., Crews, Q. E. and Walsh, P. C. (1974). Prostate carcinoma: radiation treatment of the primary and regional lymphatics. *Cancer*, **34**, 156-160.

McCullough, D. L., Prout, G. R. and Daly, J. J. (1974). Carcinoma of the prostate and lymphatic metastases. *Journal of Urology*, **111**, 65-71.

McLaughlin, A. P., Saltzstein, S. L., McCullough, D. L. and Gittes, R. F. (1976). Prostatic carcinoma: incidence and location of unsuspected lymphatic metastases. *Journal of Urology*, **115**, 89-94.

Nicholson, T. C. and Ritchie, J. P. (1976). Pelvic lymphadenectomy in prostatic adenocarcinoma. A.U.A. Annual Meeting, Las Vegas, May 1976.

Paxton, R. M., Williams, G. and Macdonald, J. S. (1975). Role of lymphography in carcinoma of the prostate. *British Medical Journal*, **1**, 120-122.

Ray, G. R., Cassady, J. R. and Bagshaw, M. A. (1973). Definitive radiation therapy of carcinoma of the prostate. A report of 15 years of experience. *Radiology*, **106**, 407-418.

Rost, A., Kelämi, A., Weber, P., Pust, R. and Taenzer, V. (1975). Proof of metastases by lymphography on prostatic carcinoma. *Urologia Internationalis*, **30**, 402-413.

Shearer, R. J., Constable, A. R., Girling, M., Hendry, W. F. and Fergusson, J. D. (1974). Radioisotopic bone scintigraphy with the gamma camera in the investigation of prostatic cancer. *British Medical Journal*, **2**, 362-365.

Wallace, D. M., Chisholm, G. D. and Hendry, W. F. (1975). T.N.M. classification for urological tumours (U.I.C.C.)—1974. *British Journal of Urology*, **47**, 1-12.

Whitmore, W. F. (1956). Hormone therapy in prostatic cancer. *American Journal of Medicine*, **21**, 697-713.

Whitmore, W. F., Hilaris, B. and Grabstald, H. (1972). Retropubic implantation of Iodine 125 in the treatment of prostatic cancer. *Journal of Urology*, **108**, 918-920.

Wilson, C. S., Dahl, D. S. and Middleton, R. G. (1976). Pelvic lymphadenectomy for staging prostatic carcinoma. A.U.A. Annual Meeting, Las Vegas, May 1976.

Zingg, E. J., Fuchs, W. A., Héritier, P. and Göthlin, J. (1974). Lymphography in carcinoma of the prostate. *British Journal of Urology*, **46**, 549-554.

The Authors

E. P. N. O'Donoghue, MB, FRCS, Senior Lecturer and Honorary Consultant Urologist.
P. Shridhar, MB, FRCS, Research Fellow.
T. Sherwood, MRCP, FFR, Consultant Radiologist.
J. P. Williams, MChir, FRCS, Consultant Urologist.
G. D. Chisholm, ChM, FRCS, Consultant Urological Surgeon and Senior Lecturer.

British Journal of Urology (1976), **48**, 697-701 ©

Urethroplasty in Context

J. P. BLANDY, S. WADHWA, M. SINGH and G. C. TRESIDDER
The London and St Peter's Hospitals, London

Most of us were brought up to believe in the precept "Once a stricture always a stricture". Gentle dilatation of the urethra was the first practical lesson any urologist had to learn, but over the last decade techniques of urethroplasty have been devised so diverse and so adaptable that almost any stricture can now be offered a permanent cure. It is now time to look again at our practice. When should we use the bougie, and when ought we to consider urethroplasty? It was only right and proper to start by being somewhat cautious in offering a new and untried operation to a patient who could be managed by regular and gentle dilatation, and over the last decade we have only offered urethroplasty to those men in whom dilatation had to be done very frequently, was followed by complications such as bacteraemia and bleeding, or was exceedingly difficult to do (Blandy 1976*a*, *b*).

During this time we have had a considerable number of men attending for regular urethral dilatation, though each case was reviewed from time to time and the question of urethroplasty discussed. To evaluate the place of urethroplasty in the whole context of the management of strictures of the male urethra we have to examine the records not only of patients who were subjected to operations on their urethral strictures but also of those who (we thought) were going on very well with intermittent dilatation.

Patients

The series under review is made up of 357 consecutive male cases attending the Department of Urology at The London Hospital and 1 clinic at St Peter's Hospital from 1965 through 1975, a period in which urethroplasty was offered only to patients who were undergoing very frequent instrumentation, or in whom instrumentation was complicated by bacteraemia, haemorrhage, or extravasation, or in whom dilatation was difficult or impossible.

It must be stated that during this period the majority of the dilatations were performed by experienced surgeons and the complications encountered during this period cannot be set down to inexperience.

129 of the whole series of 357 patients have been managed by intermittent dilatation only: 228 (64%) have undergone some form of urethroplasty. This figure however gives a distorted picture for at least 75 cases were second referrals from other centres specifically for urethroplasty: 7 of these were in fact managed by dilatation (usually after urethrotomy) and 68 were subjected to urethroplasty. Of 282 cases attending these hospitals primarily a smaller proportion—160 (57%) were offered urethroplasty: *i.e.* 57% had failed a trial of dilatation. We were interested to see how the remaining cases, who were not selected for urethroplasty, fared over the years when compared with those who underwent an operation. In making this comparison we have included patients referred from elsewhere, who were not operated on if their strictures could be

Read at the 32nd Annual Meeting of the British Association of Urological Surgeons in London, June 1976.

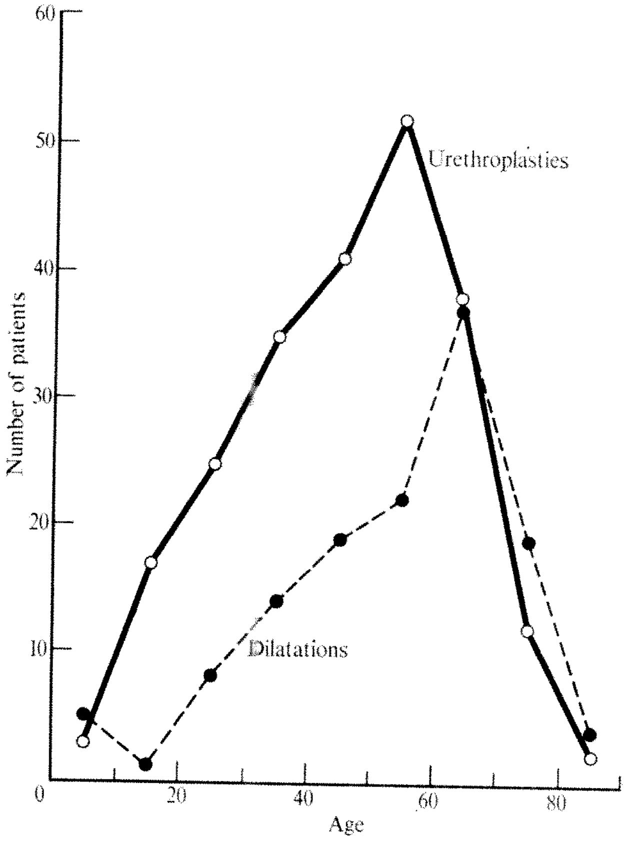


Fig. 1. Age incidence of male urethral strictures.

dilated reasonably easily. Among these 68 patients no less than 30 had previously undergone some form of urethroplasty elsewhere.

The age incidence in the 2 groups of male patients (Fig. 1) shows that we have been more willing to offer urethroplasty to younger patients, perhaps because they were more prone to the very difficult strictures which follow trauma, a point emphasised again in Table I which lists the aetiology of these strictures.

The Role of Internal Urethrotomy

Internal and external urethrotomy was used whenever it seemed appropriate. One or more internal urethrotomies were performed in no less than 18 of the patients who subsequently needed urethroplasty and in 17 of those who were afterwards managed by regular dilatation. We have never seen a single instance where urethrotomy gave a permanent cure. We have not used adjuvant

Table I

Aetiology of 357 Strictures

	Dilatation	-plasty	Total
Congenital	12	7	19
Traumatic			
accident	8	67	75
iatrogenic	75	60	135
Inflammatory			
gonorrhoea	19	62	81
tuberculosis	1	6	7
Unknown	14	26	40
Total	129	228	357

Table II

Morbidity in 129 Strictures Treated by Dilatation

Kidney	pyelonephritis 1, hydronephrosis 1, staghorn 1, nephrectomy 2	5	3·9%
Bladder	diverticula 3, stones 2, acute retention of urine 20	25	19·3%
Urethra	diverticulum 1, abscess 5, false passage 13, extravasation 3	24	18·6%
Infection	bacteraemia 6, endocarditis 1, epididymitis 11	18	13·9%

steroid therapy or prolonged indwelling catheterisation—manoeuvres which have been said to improve the results of urethrotomy.

The Complications of Intermittent Dilatation (Table II)

This may seem a formidable list of complications, but many of them occurred before we settled into a regular routine of dilatation, and 73 (57%) of the whole group had no complications at all. Nevertheless 43% of patients who were thought to be doing well had some complication, and all those men with more serious difficulties had already been selected for urethroplasty. It is against such a background that we must now review the advantages and disadvantages of urethroplasty (Table III).

The Complications and Results of Urethroplasty

Table III shows that 32 complications were noted in 228 patients undergoing urethroplasty. This does not give the whole picture: in addition, out of 146 2-stage urethroplasties, 29 (19·9%) had to have 1 or more adjustments made to the flap after the first stage and before it was ready to be closed at the second stage. Furthermore 40 out of the entire group of 228 cases needed only relatively easy operations of meatoplasty or the Denis-Browne-Swinney type of urethroplasty. In evaluating urethroplasty the real discussion focuses on the problem cases in whom the posterior urethra is involved, where the operations are specially difficult, and where particular care is

Table III

Morbidity in 228 Urethroplasties

Operative death	1	0·4%
Haemorrhage	2	0·9%
Pulmonary embolism	1	0·4%
Wound dehiscence	2	0·9%
Detachment of patch	1	0·4%
Fistula	7	3·1%
Hairball calculus	4	1·8%
Recurrent stricture	14	6·1%
Total	32	14·0%

Table IV

Methods used in 228 Urethroplasties

Site	Method of urethroplasty					
	Meatoplasty	Swinney	Island patch	Scrotal flap	Tubed flap	Others
Meatus	28	–	–	–	–	–
Penile	–	12	8	–	–	1
Posterior	–	–	32	134	11	2
Total	28	12	40	134	11	3

needed in the follow-up (Table IV). Not surprisingly, it is among these difficult cases that most of the complications are found. Many of them had had previous attempts at urethroplasty and the utmost ingenuity was needed to form a new urethra for them.

The entire toll of complications is not great when we compare them with those found in the cases treated only by dilatation.

A more pertinent question is "How often does the stricture come back after urethroplasty?" So far only 14 (6·2%) cases have come back with restenosis and 2 of these men had suffered at least 1 further attack of gonorrhoea. Of these failures 2 of them are dilated occasionally; 11 have either had 1- or 2-stage urethroplasties performed again usually for an annular stenosis at 1 or other end of the first urethroplasty: 2 have had a successful transpubic repair (Waterhouse *et al.*, 1974).

There has been a remarkable freedom from incontinence among these men: even in the 29 who had to have a prostatectomy as well as a high urethroplasty in which a skin inlay was placed right across what one assumes to be the external sphincter, only 3 were permanently incontinent: only 1 of them had been dry before his urethroplasty, and the other 2 had been wet ever since their previous prostatectomies. There was also 1 man who was incontinent before his urethral stricture had been operated on and who became dry afterwards. It is interesting to note that Colapinto and McCallum (1976) have had similar results after prostatectomy as well as sphincter-crossing urethroplasty.

There were 12 out of 157 men who were intended to go through a 2-stage operation, but who did not complete the second stage. 2 were found to have developed metastatic carcinoma of the lung between the first and second stages. 9 were so happy with the result of the first stage that they refused any more operations and 1 recent patient is at present waiting for his second stage operation.

Discussion

We were disturbed to find so many serious complications among patients who we thought had been well managed by intermittent dilatation. It is very likely that the record of only 5 episodes of bacteraemia in this series is a considerable underestimate, as is the estimated number of 13 false passages. 9 patients required very frequent or difficult dilatations: 3 had refused operation and the remaining 6 were too old or unfit to be offered one.

The outcome of this decade of experience with urethroplasty shows it to have a failure rate of about 6%, but about 20% have to undergo a revision between the first and second stages in cases where a 1-stage operation cannot be done. But these were all men who had impassable or very difficult and complicated strictures for whom dilatation had been attempted and had failed. No less than 32 of the urethroplasty series arrived with a suprapubic tube in position; 2 of these had been worn for more than 5 years. It seems likely that urethroplasties in less difficult cases would be even less likely to have significant postoperative complications.

At the conclusion of this review we have had to reconsider our policy. Perhaps we have been too stringent in our indications for urethroplasty; maybe it should be offered sooner, and upon less strict indications than in the past, for these results suggest that the operations of urethroplasty have stood the test of time and are in many cases a safer alternative than a lifetime of dilatation.

References

BLANDY, J. P. (1976*a*). Urethroplasty in males. In *Recent Advances in Urology 2*, ed. W. F. Hendry. Churchill Livingstone, chap. 10, pp. 208-231.

BLANDY, J. P. (1976*b*). Urethral stricture and carcinoma. In *Urology*, ed. J. P. Blandy. Oxford, Blackwell Scientific, **2**, chap. 39, pp. 1014-1048.

COLAPINTO, V. and MCCALLUM, R. W. (1976). Urinary continence after repair of membranous urethral stricture in prostatectomised patients. *Journal of Urology*, **115**, 392-396.

WATERHOUSE, K., ABRAHAMS, J. I., CAPONEGRO, P., HACKETT, R. E., PATIL, U. B. and PENG, B. K. (1974). The transpubic repair of membranous urethral strictures. *Journal of Urology*, **111**, 188-190.

The Authors

J. P. Blandy, DM, MCh, FRCS, Professor of Urology (London Hospital), Consultant Surgeon (St Peter's Hospitals).

S. Wadhwa, MBBS, MS (General Surgery), MCh (Urology), Visiting Commonwealth Fellow to Department Urology at London Hospital. (Now Assistant Professor Urology at All India Institute of Medical Science.)

M. Singh, FRCS, Consultant Urologist, Whipps Cross Hospital.

G. C. Tresidder, FRCS, Consultant Urologist at London Hospital. (Now Lecturer in Anatomy, University of Southampton.)

British Journal of Urology (1976), **48**, 703-707 ©

Hypospadias—Problems of Postoperative Fistulae Formation and a Modified 2-Stage Procedure to Reduce These

P. J. B. SMITH, P. L. G. TOWNSEND, J. R. W. HILES and J. R. BRYSON

Department of Urology, St Martin's Hospital, Bath and Department of Plastic Surgery, Frenchay Hospital, Bristol

Children with hypospadias are often initially referred to a plastic surgeon because of his long-standing interest in this technically difficult problem. Urologists, expressing an interest, are also likely to have an increasing number of cases referred. The intricacy of management has often resulted in close co-operation between urologists and plastic surgeons. A retrospective review has been made of 147 cases of hypospadias managed by 10 different surgical firms over a 10-year period. The extent of the hypospadias both in terms of the position of the meatal opening and the degree of chordee, reflected that of other large series (Welch, 1969).

Patients

From a study of the operative techniques employed in 147 children it can be seen that in many of these, the deformity was minimal and only a minor surgical procedure such as circumcision or meatotomy was necessary (Table I). In the remainder, a variety of 1- and 2-stage repair operations have been performed. In the assessment of postoperative complications following these repair operations, a depressingly high incidence of fistula formation was noted (Table II.)

Table I

Operative Techniques for Hypospadias

Denis Browne	25
Duplay	16
Ombredanne	16
Broadbent	13
Mustarde	8
McIndoe	10
Circumcision	15
Meatotomy	25
Chordee correction	8
Not specified	11
Total	147

Table II

Postoperative Complications of Hypospadias Repairs

Fistulae	55
Stenosis	14
Recurrence of chordee	8

Read at the 32nd Annual Meeting of the British Association of Urological Surgeons in London, June 1976.

Table III

Urethral Casts made after Hypospadias Repairs with Fistula Complication

Denis Browne	8
Duplay	9
Mustarde	3
Broadbent	5
Nicol	2
Cecil	1
McIndoe	2
Others	3
Total	33

Methods

In an attempt to obtain more information on the postoperative fistulae complicating hypospadias repair, a series of silicone urethral casts have been taken by one of us as previously described (Townsend, 1975).

Results

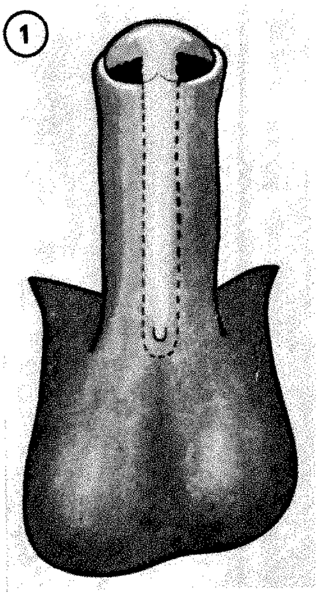
Casts have been taken from 33 cases with postoperative fistulae occurring after a wide variety of repair procedures (Table III). 16 casts from 29 different cases of these casts showed dilatation and overhanging pouches of reconstructed urethra at the junctional area where the normal urethra joined the reconstructed one. This was particularly evident after Denis Browne repair. In 21 out of 29 different cases the fistulae had formed within ½ cm or less of this same junctional area.

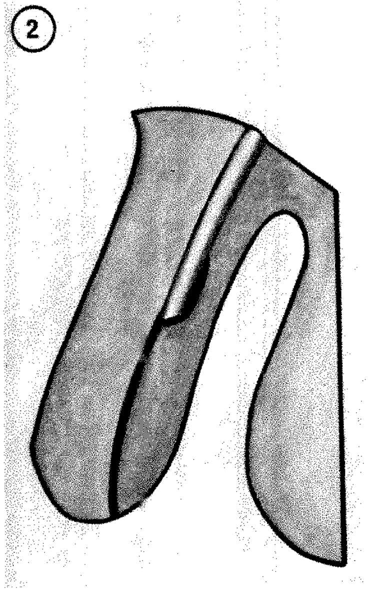
As well as distal urethral stenosis remaining after inadequate meatotomy, they also revealed skin bridges in 4 cases. These bridges were present at the base of the fistula. In 5 more cases there was a marked skin crest in a similar situation. These casts also revealed a tendency in the tubed flap Broadbent repair to adopt a snake-like oblique outline. A constricting effect was demonstrated in the tubed flap of a Mustarde repair in the area where the skin-tube was passed through the glans.

Discussion

The overhang described at the junctional area can best be explained by a study of the basic design of the Denis Browne repair (1949). As can be seen in a copy of an original drawing (Fig. 1) a U-shaped part of the skin strip is left to epithelise just proximal to the original meatal opening —shown more clearly in the lateral view (Fig. 2). After epithelisation this area tends to become associated with an overhang on the ventral surface of the distal end of the junction between the original and reconstructed urethra (Fig. 3). The provision of this U-shaped piece of skin in the original incision would seem to be the most likely cause for this overhang developing. Such a U-shaped incision is a common feature of design in a large number of repair procedures including as well as the Denis Browne, the Duplay (1879), Broadbent (1961) and Mustarde (1971) repairs.

In postoperative assessment of such a case, this overhang may often feel like a urethral diverticulum when a probe is passed. Similar dilatation may be caused or complemented by the distal urethral stenosis due to the previously mentioned inadequate meatotomy. This stenosis, as well





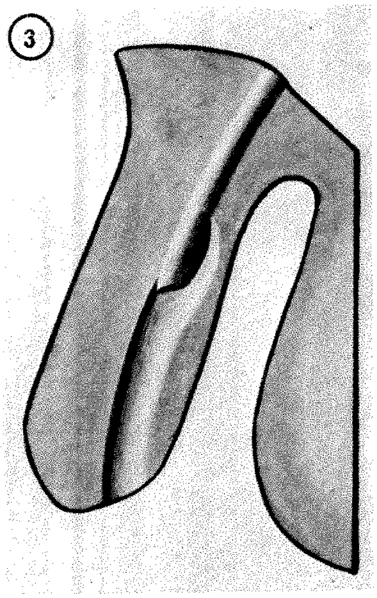


Fig. 1. Denis Browne repair—ventral view of penis to demonstrate design of skin strip to be left to form epithelial tube. Note U-shaped flap of skin proximal to meatal opening.

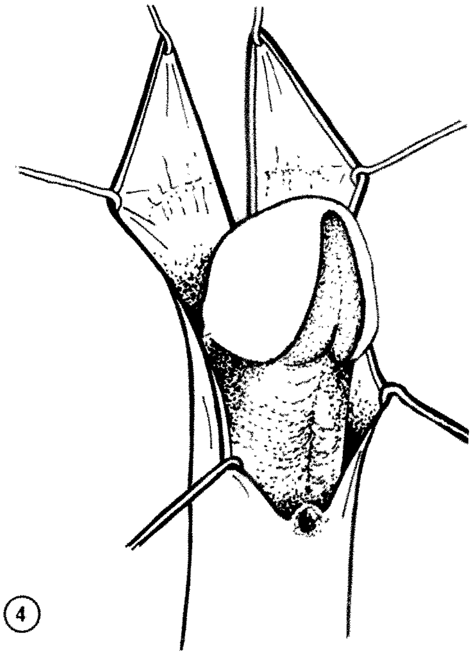
Fig. 2. Denis Browne repair—section of penis showing buried skin strip extending proximal to original meatal opening.

Fig. 3. Denis Browne repair—section of penis showing late stage of repair with epithelisation of skin tube and the development of a dilatation and overhang at the junctional area, due to previously formed U-shaped flap of skin, proximal to original meatus.

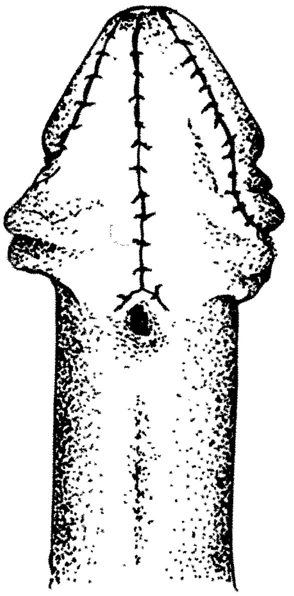
as obstructing flow may also lead to turbulence of urine, a phenomenon also produced by the skin bridges and crests previously noted. Turbulence of urine in the distal reconstructed urethra may lead to increased sheering stresses and a tendency to breakdown, with fistula formation in the proximal reconstructed urethra, in the region of dilatation and overhang at the junctional area.

These casts have helped to focus attention on this important junctional area in the design of hypospadias repairs. With regard to initial design, the U-shaped piece of skin left proximal to the urethral opening is in many cases unnecessary, for instance in the Denis Browne or Duplay type of repair. In these operations the skin can be tapered down to the existing urethral opening without difficulty. However, when this area forms the base of a flap as in the Broadbent or Mustarde repairs, it is difficult to taper down due to the possibility of damaging the vascular supply of the flap by this dissection. An adequate meatotomy must always be carried out, care being taken to extend the incision back down the urethra so as to include any extension of the stenosis into the urethra. Where tube skin is brought to the tip of the glans it would seem best to insert it into the glans rather than try and burrow through it.

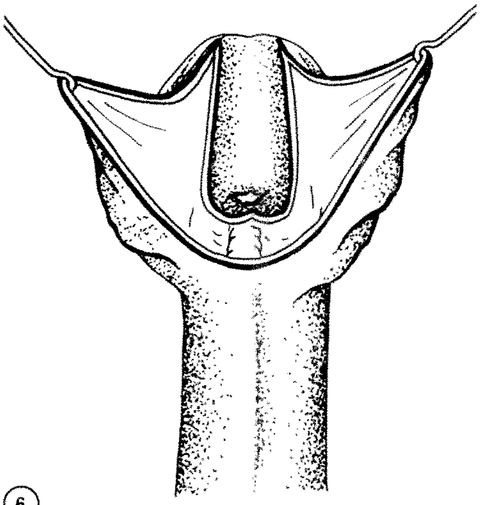
As a result of these findings and our continued co-operation in the management of hypospadias cases we would now favour a 2-stage repair where it is considered that surgical correction is necessary. The first stage ensures an adequate meatotomy and complete correction of chordee—an essential feature of any hypospadias repair. At the same time, by employing the technique described by Blair and Byars (1938) we divide the prepuce and transpose preputial skin into the gap created by the chordee release (Fig. 4). In this way we ensure that fine textured, hairless skin is transposed on to the ventral surface of the penis to be employed subsequently for the urethral reconstruction in the second stage procedure (Fig. 5). This first stage is usually carried out when



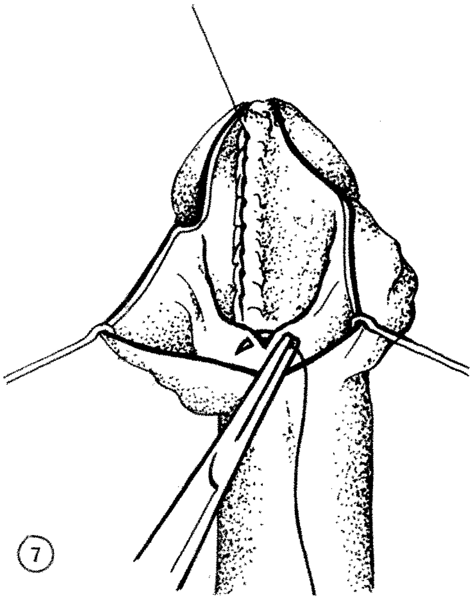
④



⑤



⑥



⑦

Fig. 4. First stage repair of hypospadias. Chordee corrected, meatotomy performed, prepuce divided and skin flaps being brought round.

Fig. 5. First stage repair—preputial skin flaps rotated into position and covering gap left by correction of chordee.

Fig. 6. Second stage hypospadias repair. Preputial skin incised to produce skin tube. Care being taken to prevent proximal U-shaped flap.

Fig. 7. Second stage repair hypospadias. Skin tube of new urethra sewn with continuous 6-0 Dexon, commencement of closure of subareolar sandwich layer, operation completed by subcuticular closure of penile skin.

the child is 2 years old and the second stage of urethral reconstruction approximately 6 to 12 months later. This reconstruction is effected along the lines of the Duplay repair (1879). In this technique, a tube flap is raised using the previously transposed preputial skin, care being taken to avoid creating a U-shaped flap of skin, as mentioned above (Fig. 6). Closure of the tissues is carried out in 3 layers (Fig. 7). The first of these is a subepithelial layer for the urethral tube, care being taken not to enter the lumen of the reconstructed urethra with this stitch. Above this is a subareolar sandwich layer, and finally a subcutaneous closure of the penile skin. As in the first stage great importance is attached to tissue handling. 6-0 Dexon is the suture used. Suprapubic drainage is employed after the second stage, care also being taken to splint the penis in an erect position using Micropore dressing.

Conclusion

It is unlikely that the incidence of fistula formation with any particular type of repair can ever be reduced to zero. However, it is hoped that with the greater attention paid to certain anatomical features a better understanding can be made of the problems involved in the design of hypospadias repairs and the subsequent treatment of any complications. We believe that when surgical repair of hypospadias is necessary the 2-stage repair described above, with preputial skin transposition and a tube urethral repair, seems to offer a simple and effective procedure. This technique would seem to be eminently suitable to the wide range of experience from consultants to training grades in both urology and plastic surgery departments.

Summary

A retrospective review of hypospadias repair reveals a high incidence of postoperative fistula and stenosis. Further studies using Silicone casts have revealed a potential cause for the occurrence of these complications.

The close co-operation between urologists and plastic surgeons has resulted in a greater awareness of the surgical problems and the development of a simplified 2-stage technique which it is hoped will reduce these.

References

Blair, V. P. and Byars, L. T. (1938). Hypospadias and epispadias. *Journal of Urology*, **40**, 814-825.

Broadbent, T. R., Woolf, R. M. and Toksu, E. (1961). Hypospadias one stage repair. *Plastic and Reconstructive Surgery*, **27**, 154-159.

Browne, D. (1949). Operation for hypospadias. *Postgraduate Medical Journal*, **25**, 367-372.

Duplay, S. (1879). Nouvelle méthode opératoire applicable au traitement de l'hypospadias perineo-scrotal. *Archives Genérales de Médicine*, **23**, 657-662.

Mustarde, J. C. (1971). Hypospadias in the distal third of the penis. *Transactions of the Fifth International Congress of Plastic and Reconstructive Surgery*. Melbourne: Butterworths, pp. 356-374.

Townsend, P. L. G. (1975). Silicone rubber casts of the distal urethra in studying fistula formation and other hypospadias problems. *British Journal of Plastic Surgery*, **28**, 320-323.

Welch, K. J. (1969). Hypospadias. In *Pediatric Surgery*, ed. W. T. Mustard and others, 2nd ed., Vol. 2. Chicago: Year Book Medical Publishers, pp. 1313-1332.

The Authors

P. J. B. Smith, FRCS, Consultant Urologist, St Martin's Hospital, Bath.
P. L. G. Townsend, FRCS, Senior Registrar in Plastic Surgery, Frenchay Hospital, Bristol.
R. W. Hiles, FRCS, FRCSE, Consultant Plastic Surgeon, Frenchay Hospital, Bristol.
J. R. Bryson, FRCS, S.H.O. in Plastic Surgery, Frenchay Hospital, Bristol.

Note—It has been necessary to reduce the size of this paper from the work originally presented. Further details relating to the use of the Silicone casts can be obtained from one of us (P. L. G. T.). More details of the operation technique, including drawings, can also be obtained (from R. W. H.).

British Journal of Urology (1976), **48**, 709-717 ©

Plasma Gonadotrophic Hormones, Testicular Biopsy and Seminal Analysis in the Men of Infertile Marriages

J. P. PRYOR, R. C. B. PUGH, K. M. CAMERON, J. R. NEWTON and W. P. COLLINS

Departments of Urology and Pathology, St Peter's Hospitals and the Institute of Urology and the Departments of Urology and Gynaecology, King's College Hospital

The investigation of male infertility leaves much to be desired and the search continues for those factors that are of diagnostic or therapeutic importance in men with azoospermia or oligozoospermia. Radioimmunoassay techniques have made it possible to measure human plasma gonadotrophins and this study was performed to see if the hormone levels were useful in the clinical management of infertile men.

In the past, diagnosis of an obstructive lesion in azoospermic men was made by the clinical assessment of testicular size and upon the result of a testicular biopsy and vasogram performed under a general anaesthetic. It would therefore be a great advantage to have a non-invasive procedure to show which men might benefit from operative treatment.

The present treatment of oligozoospermic men is unsatisfactory, and, whilst it is true that drug therapy may improve the sperm count in some, there has been a remarkable lack of clinical trials to show the effectiveness of any drug. Furthermore the choice of drug for therapy is made on an empirical basis and it would be beneficial to identify which oligozoospermic men might benefit from specific treatment.

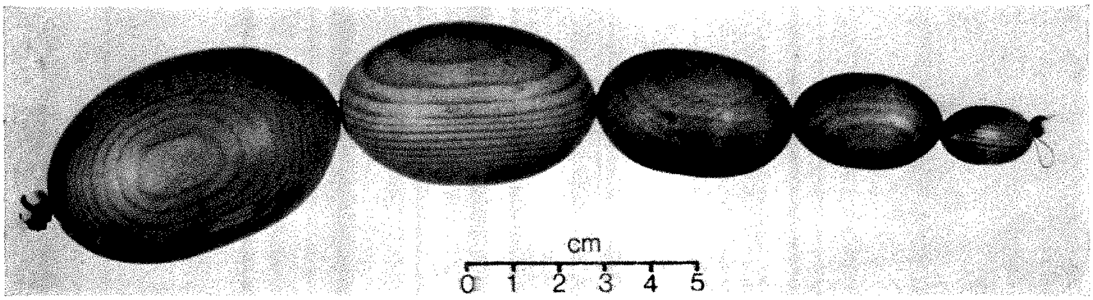


Fig. 1. Graduated rosary of wooden ovoids for measuring testicular length.

Methods

261 male partners of infertile marriages attended the Andrology Clinic at St Peter's or King's College Hospitals in the period January 1975 to April 1976. This report is concerned primarily

Read at the 32nd Annual Meeting of the British Association of Urological Surgeons in London, June 1976.

Table I

Technical Details of the Gonadotrophic Hormone Assays

Hormone (units)	Labelled tracer	Immunogen	Reference preparation	Separation technique
Luteinising LH (U/L)	125-I (IRC-2)	HP-LH	MRC 68/40 (77·1 u/ampoule)	DA
Follicle stimulating (U/L)	125-I (MRC 71/333)	HP-FSH	MRC 69/39 (32·8 u/ampoule)	DA

Table II

Mean Values for Testicular Size, FSH and LH Related to the Mean Johnsen Score of the Testicular Biopsy

		Mean		
Mean Johnsen score	Number	Testicular size (cm)	FSH (U/L)	LH (U/L)
<2·0	32	3·0±1·1	19·3±11·9	14·0±10·2
2·1-6·0	17	3·9±0·9	12·0±10·9	15·4±14·0
6·1-8·0	7	3·9±0·9	3·9± 3·2	6·3± 1·6
>8·1	27	4·8±0·7	1·7± 0·5	5·9± 5·4
Fertile men	46	–	1·8± 1·5	7·0± 3·1

with those patients who underwent a testicular biopsy and whose plasma gonadotrophic hormone levels were known.

The men were generally fit and well and in the age range of 20-40 years. Testicular size was assessed clinically and the minimum length recorded by comparison with a rosary of graduated wooden ovoids 2 to 6 cm long (Fig. 1).

Semen analysis was performed on 2 occasions, at least 3 days after the previous emission, and the results quoted are for the mean total sperm count per ejaculation. Other variables in the sperm count are not considered in this paper which is particularly concerned with spermatogenesis.

The testicular biopsy was performed under general anaesthetic and at the same operation for azoospermic men the epididymis was inspected for evidence of obstruction and a vasogram performed. The biopsy was placed in Bouin's solution prior to routine embedding and sectioning before staining with haematoxylin and eosin. Spermatogenesis was assessed and the results scored using Johnsen's method (Johnsen, 1970). The mean Johnsen score gives an overall estimate of the degree of spermatogenesis but any score needs to be interpreted in the light of the full profile of the spermatogenesis in each tubule.

The levels of follicle stimulating hormone (FSH) and luteinising hormone (LH) in peripheral venous plasma were measured by radioimmunoassay methods. The labelled antigens, antisera and reference preparations are shown in Table I. In several patients multiple estimations were obtained and there was little variation in the levels recorded. The normal range for the laboratory

Table III

The Relationship between Testicular Size and the Mean Johnsen Score of the Testicular Biopsy in Azoospermic Men

Number of patients	Testicular size (cm)	Mean Johnsen score			
		<2·0	2·1-6·0	6·1-8·0	>8·1
14	2	14			
33	3	16	12	3	2 (6%)
35	4	18	6	2	9
45	5	3	8	2	32
3	6	(6%)			3

was obtained by measuring the levels in 46 men of recently proven fertility who had attended for a vasectomy.

Results

A. Azoospermic Men

There were 93 men with a complete absence of spermatozoa in the ejaculate and they had a wide range in the size of their testes and the appearance of the testicular biopsy. The results are therefore subdivided, according to the mean Johnsen score of the better testis, into 4 groups and the mean results of testicular size, FSH and LH are summarised in Table II.

The 37 patients with mean Johnsen scores greater than 8·1 are considered to have obstructive azoospermia. Evidence for an obstructive lesion was obtained from the vasogram or from inspection of the epididymis but in some patients the block was in the rete testis.

Testicular Size

Table II shows that the mean testicular size of patients with obstructive azoospermia was 1·8 cm longer than those men with absent spermatogenesis (mean Johnsen score <2·0). However, Table III shows that clinical examination of testicular size does not give a sufficiently reliable guide to the degree of spermatogenesis as 6% of men with small testes show "normal" spermatogenesis and in a similar proportion of men with normal sized testes there was no spermatogenesis.

No account had been taken of the consistency of the testicle as it is difficult to quantify. It is also a poor guide to spermatogenesis as can be seen from the patient with a small (3 cm), soft testicle on one side and a normal testicle (5 cm and firm) on the other side. The mean Johnsen score was similar on both sides (3·8 and 3·7).

Follicle Stimulating Hormone

The mean level of the FSH fell as the appearance of the testicular biopsy showed increasing spermatogenesis (Fig. 2). The mean was grossly elevated for those patients where the mean Johnsen score was less than 6·0 and was normal for those with obstructive azoospermia. If the test is to be of clinical value the individual results must be studied and these are shown in Figure 3.

29 of the 32 patients with FSH levels in the normal range had an obstructive azoospermia. 2 of the patients had arrested spermatogenesis (mean Johnsen scores 4·6 and 4·8) and in the other there was a complete absence of spermatogenesis (Johnsen score 2·0) on both testicular biopsies. A further hormone assay on a separate blood sample in this patient also showed a normal FSH level and this probably means that there was a pituitary defect which was not apparent clinically.

Grossly elevated FSH levels (more than twice the upper limit of the normal range) were found

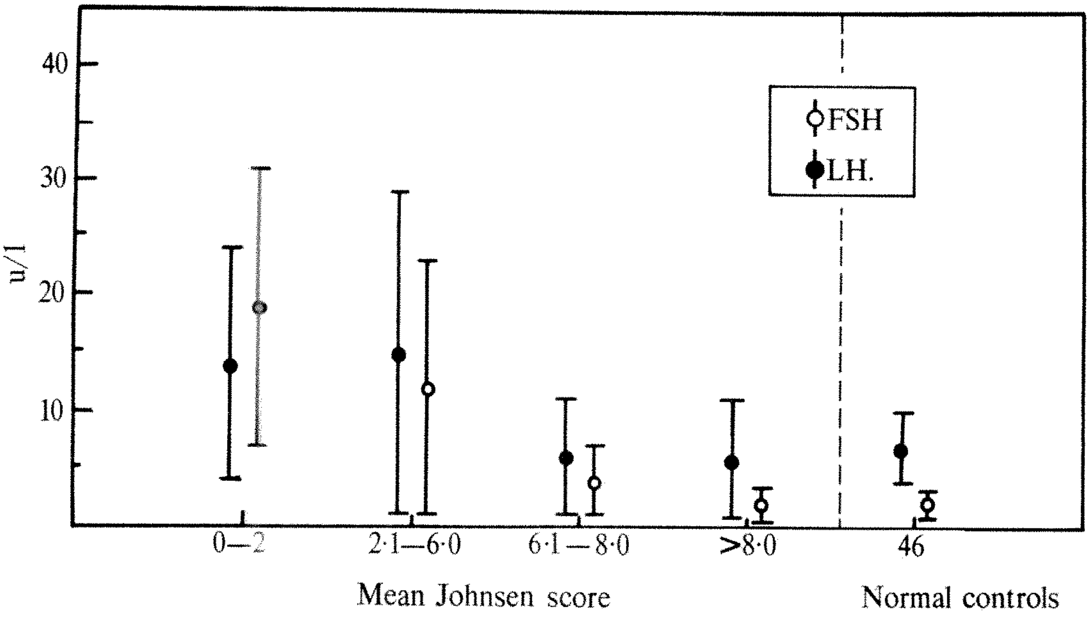


Fig. 2. The relationship between the mean FSH and LH levels and the mean Johnsen score of 93 azoospermic men.

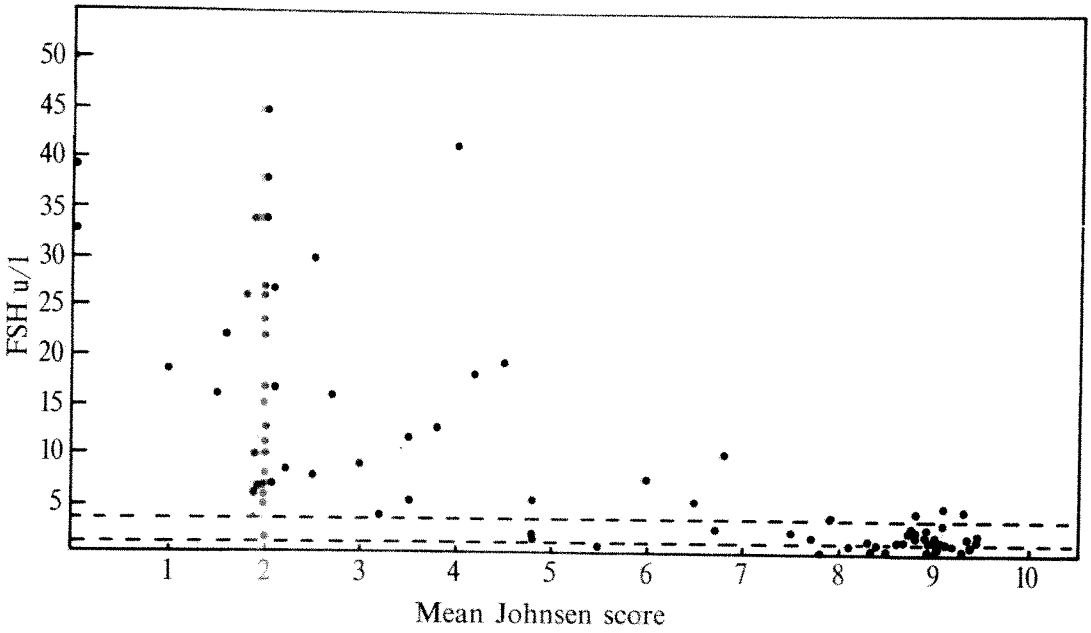


Fig. 3. FSH levels in 93 azoospermic men.

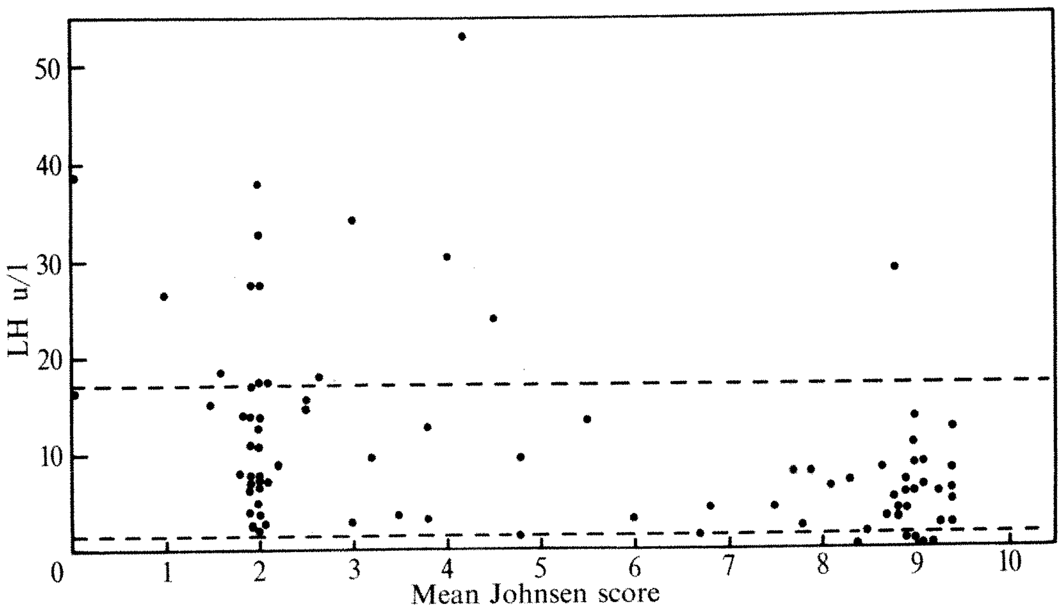


Fig. 4. LH levels in 93 azoospermic men.

in 37 patients. In 26 of these there was no spermatogenesis, and in all but 1 of the remainder there was gross impairment of spermatogenesis and the Johnsen score was less than 6·0. A mild elevation of FSH occurred in all groups and it is of interest that 3 of the 4 patients with obstructive azoospermia had one testis absent or atrophic.

Sub-normal FSH levels were found in 10 patients and 7 of them had obstructive lesions. The testicular biopsy in 3 patients showed arrested spermatogenesis and 1 of these after the first 6 weeks of treatment with H.M.G. (Pergonal) is no longer azoospermic.

Luteinising Hormone

The mean level of luteinising hormone (LH) was higher in those patients with a mean Johnsen score of less than 6·0 (Fig. 2). The individual results are shown in Figure 4 and it is apparent that most levels were within the normal range. However, 16 of the 17 patients with levels above the normal range had mean Johnsen scores of less than 6·0. This suggests a primary testicular defect which affects all elements of the testes.

B. Oligozoospermic Men

Analysis of the results in the 65 oligozoospermic men is more difficult as many variables of the seminal fluid are of importance in fertility (*e.g.* volume and sperm density and motility). There is no agreement as to the normal values but the Comité International d'Andrologie (CIDA) define oligozoospermia as less than 40 million sperms/ml and the normal volume to be 2-6 ml. In the present series 23 patients had a *total* sperm count of less than 1 million sperms, 14 had 1-10 millions and 25 had 11-100 millions. 2 patients with counts of 150 and 350 millions had varicoceles and a third, with a count of 150 millions, had only 10% of motile sperms in each specimen.

The mean values for the testicular size, Johnsen score, FSH and LH in oligozoospermic men are shown in Table IV.

Table IV

Mean Values for Testicular Size, Johnsen Scores, FSH and LH according to the Total Sperm Count

Mean total sperm count (million sperms/ejaculate)	Number	Testicular size (cm)	Mean Johnsen score	FSH (U/L)	LH (U/L)
<1	23	4·1±0·8	7·2±2·1	4·5±5·1	6·1 ± 4·2
1-10	14	4·5±0·9	7·6±0·9	2·8±3·1	8·7 ±12·1
>11	28	4·3±0·8	8·6±1·4	2·5±2·0	5·32± 4·0

Table V

The Relationship between Testicular Size and the Mean Johnsen Score in the Testes of Oligozoospermic Men

Size (cm)	Number	Mean Johnsen score <2·0 (number of patients)	2·1-6·0	6·1-8·0	>8·1
3	18	2	3	3	10 (55%)
4	33		3	6	24 (72%)
5	29	1	1	5	22 (73%)

Testicular Size

The mean testicular size was not related to the total sperm count, although a greater proportion of patients with normal sized testes had a sperm count in excess of 10 millions per ejaculate. The relationship between testicular size and the histology is shown in Table V and it can be readily seen from the Table that clinical examination of size offers only an approximate guide to spermatogenesis.

Testicular Biopsy

The average mean Johnsen scores of the testicular biopsies (Table IV) was higher with regard to increasing total sperm counts. However, 1 patient with a poor biopsy (Johnsen score 2·5 and 2·2) had a total sperm count of 16 millions and another with less than a million sperms and Johnsen scores of 2·2 and 2·0 has subsequently reported his wife to be pregnant. It is important not to rely upon the mean Johnsen score alone but to examine the whole profile of spermatogenesis on the testicular biopsy. Conversely, 8 patients with mean Johnsen scores in excess of 8·9 had total sperm counts of less than a million and it is possible that in these patients an undetected obstructive element may exist.

FSH and LH Levels

The mean results for each group are shown in Table IV. These show that the mean FSH levels were elevated in severe oligozoospermics but were raised to a lesser extent in all groups. In contrast the LH levels were normal in all groups.

Figure 5 shows that there was considerable variation of the FSH and LH levels in all the oligozoospermic men and this may be a useful method of identifying those patients who might respond to specific treatment. 80% of the LH levels were within the normal range.

C. Men with Varicocele

17 of the oligozoospermic men had varicoceles and the mean Johnsen score of the left testis was 8·4 (range 6·2 to 9·2). In 4 patients a bilateral testicular biopsy was performed and on each occasion the mean Johnsen score of the right testicle was slightly higher (0·2, 0·3, 0·3 and 0·6). An interesting finding was that 9 of the 17 patients with varicoceles had FSH levels above the normal range. This may be a significant factor in aetiology of the infertility associated with varicocele.

D. Bilateral Testicular Biopsy

The lack of precision in the relationship between the testicular biopsy and the size of the testes will be of no surprise to many clinicians. It is often the custom to biopsy the "better" testis and the results obtained in those patients with bilateral biopsies are shown in Table VI.

In 11 (18%) men the results of the bilateral testicular biopsy were significantly different on both sides. The mean Johnsen scores of each of these patients is therefore given in Table VII and it is of interest that 1 patient's wife is pregnant, despite the biopsy on 1 side showing germinal aplasia. These findings once again raise the question of bilateral biopsies.

Discussion

The clinical estimation of testicular size gives a poor guide to spermatogenesis and if testicular biopsy is considered necessary it should be performed on both sides. Fortunately not all azoospermic men require a testicular biopsy because as a result of the gonadotrophin hormone assays it is possible to identify a group of azoospermic men who do not need further investigation.

For many years it has been known that FSH is related to spermatogenesis and that LH, although it is primarily concerned with testosterone production, has a supporting role in establishing spermatogenesis. There has been much speculation and conflicting views as to which stage of spermatogenesis is related to the inhibition of FSH production. Franchimont *et al.* (1972) suggested that FSH was elevated in those cases of azoospermia where gametegenesis was arrested prior to spermatid differentiation but other workers disagree. The subject is still open to speculation as can be seen in the recent review by Franchimont and Burger (1975). In the present

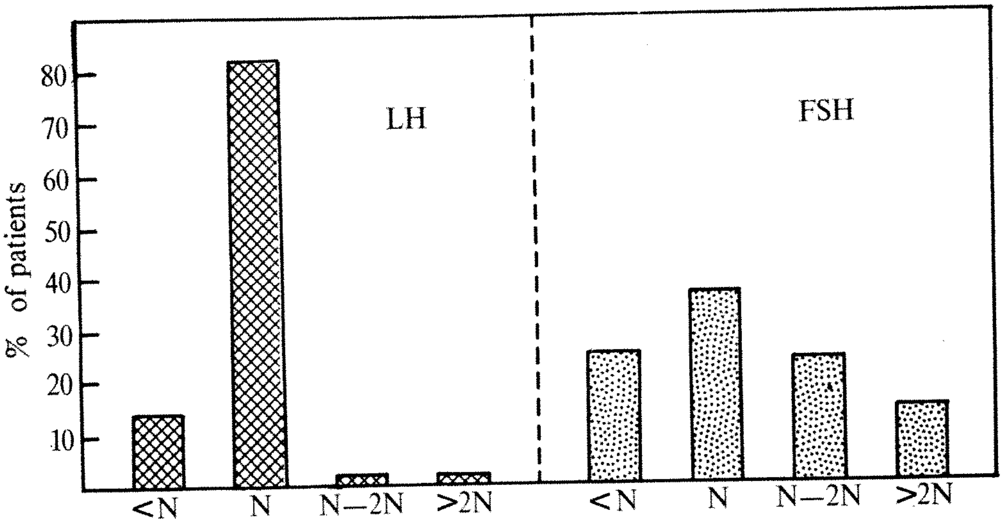


Fig. 5. The percentage distribution of the gonadotrophic hormones in oligozoospermic men.

Table VI

Results of Bilateral Testicular Biopsies in 62 Infertile Men

A. Biopsy the same on both sides	
testes equal in size	49
testes unequal in size (3 and 5 cm)	1
B. Biopsy different on both sides	
testes unequal in size	2
testes equal in size	10

Table VII

Significant Differences in the Results of Bilateral Testicular Biopsies

Azoospermia		Oligozoospermia	
Testicular size (cm)	Mean Johnsen score	Testicular size (cm)	Mean Johnsen score
3/3	8·9/4·0	5/5	9·3/3·5
5/5	2·2/2·0	3/3*	6·9/4·3
3/3	2·7/2·0	4/5†	2·2/2·0
3/3	3·2/2·0	3/3	5·7/2·0
3/3	3·5/2·0	5	6·5/2·0
3/5	3·8/3·7		

* Testis soft. † Wife pregnant.

series of 93 azoospermic men almost all men with grossly elevated FSH levels had mean Johnsen scores of less than 6·0. However, in 16 of these men the testicular biopsy showed spermatogenesis proceeding to the spermatid stage (in 3 men) or with spermatozoa formation (in 13 men).

From the clinical standpoint it is safe for the wives of those men with grossly elevated levels of FSH (more than twice the normal range) to be referred for artificial donor insemination or for adoption according to the couple's wish. Men with FSH levels of less than twice the upper limit of normal should be explored with a view to correcting any obstructive element at the time of the initial operation. This obviates a fruitless second operation for those men with absent vasa and/or a block at the level of the rete testes.

The control of FSH is still not fully understood but it has been postulated that another hormone (inhibin) is produced in the testes to inhibit FSH production. It is of interest that patients with azoospermia and absent or atrophic testes, often have elevated FSH levels as did half the patients operated upon for varicoceles. Could it be that the stasis of blood in the venous plexus around the testis is the cause of infertility in patients with varicoceles? The relative failure of "inhibin" release into the general circulation may account for the elevated FSH in circulating plasma and a local decrease in FSH may account for the appearance of immature forms in the semen of men with varicoceles.

The wide range of FSH levels in oligozoospermic men suggests the control of FSH secretion is complicated and that many factors contribute to the lack of fertility in these men. The management of oligozoospermia is haphazard and in most series, regardless of the drug used, pregnancy rates of about 20% occur during the first year or so of treatment. The Fertility Investigation Group (FIG) based at the Institute of Urology are currently undertaking a controlled trial of arginine and fluoxymesterolone in the treatment of oligozoospermic men. The results of this trial, particularly when correlated with the gonadotrophic assays, will be of great interest.

Summary

The first step in the investigation of infertile men is to obtain 2 seminal analyses 3 days after the previous ejaculation.

Clinical assessment of testicular size is an unreliable means of assessing spermatogenesis and is best done by performing bilateral testicular biopsies. Azoospermic men with grossly elevated FSH levels should be advised to consider AID or adoption. Those with normal or mildly elevated FSH levels should undergo testicular exploration in an attempt to correct an obstructive lesion.

Azoospermic men with subnormal FSH levels may have an isolated hormone defect which will respond to treatment with Pergonal.

Different treatment programmes for oligozoospermic men depending on the results of the FSH and LH assays may lead to a more rational approach to therapy.

Infertility associated with varicocele may possibly be associated with a local disturbance of "inhibin" and FSH concentrations.

References

Franchimont, P., Millet, D., Vendrely, E., Letawe, J., Legros, J. J. and Netter, A. (1972). Relationship between spermatogenesis and serum gonadotropin levels in azoospermia and oligospermia. *Journal of Clinical Endocrinology and Metabolism*, **34**, 1003-1008.

Franchimont, P. and Burger, H. (1975). *Human Growth Hormone and Gonadotrophins in Health and Disease*. Amsterdam: North Holland, pp. 157-166.

Johnsen, S. G. (1970). Testicular biopsy score count. *Hormones*, **1**, 2-25.

The Authors

John P. Pryor, MS, FRCS, Consultant Urologist, King's College and St Peter's Hospitals.
R. C. B. Pugh, MD, FRCPath, Consultant Pathologist, St Peter's Hospitals.
K. M. Cameron, MRCPath, Senior Lecturer in Pathology, Institute of Urology.
J. R. Newton, MRCOG, Senior Lecturer in Obstetrics and Gynaecology, King's College Hospital.
W. P. Collins, DSc., FRIC, Reader in Biochemical Endocrinology, King's College Hospital.

Reprints from: John P. Pryor, St Peter's Hospital for Stone, Henrietta St., London WC1.

JOURNAL OF MEDICAL MICROBIOLOGY

A Journal of the Pathological Society of Great Britain and Ireland

Edited by J G Collee, M T Parker and H Stern

The aim of the Journal is to publish papers on all aspects of microbiology - bacteriology, protozoology, virology, mycology and immunology - insofar as they are applicable to human or veterinary medicine and advance knowledge in these fields.

Published quarterly in February, May, August and November

Volume 10, 1977

Annual subscription	£17.00	USA $40.00
Single numbers	£4.50	USA $11.00

Orders to: Longman Group Ltd., Journals Division,
43/45 Annandale Street, Edinburgh EH7 4AT.

All orders must be accompanied by the appropriate remittance.

Longman

AUTHOR INDEX

Abatangelo, G., jt. author. *See* Pagano, F.
Ablin, R. J. Serum antibody in patients with prostatic cancer, 355
Abrams, P. H., Roylance, J. and Feneley, R. C. L. Excretion urography in the investigation of prostatism, 681
Allan, D. M. Recurrent transitional cell carcinoma complicating ileal conduit, 60
Altwein, J. E., jt. author. *See* Orestano, F.
Amin, H. A. Experience with the ileal ureter, 19
Andersen, J. T. and Bradley, W. E. Abnormalities of detrusor and sphincter function in multiple sclerosis, 193
Andersen, J. T. and Bradley, W. E. Bladder and urethral innervation in multiple sclerosis, 239
Andersen, J. T. and Bradley, W. E. Detrusor and urethral dysfunction in prostatic hypertrophy, 493
Andersen, J. T. and Bradley, W. E. The urethral closure pressure profile: a new technique using gas and simultaneous EMG-recording from the urethra, 341
Anderson, C. K., jt. author. *See* Vijayan, P.
Antony, A. J., jt. author. *See* Thomas, J. A.
Ardran, G. M., jt. author. *See* Ramsden, P. D
Arkell, D. G., jt author. *See* Hughes, M. A.
Ashken, M. H., jt. author. *See* Crisp, J. C.
Avidor, I., jt. author *See* Fischelovitch, J.
Awad, S. A. and Downie, J. W. Relative contributions of smooth and striated muscles to the canine urethral pressure profile, 347

Babu, A. S., jt. author. *See* Sasidharan, K.
Bagley, F. H. and Davidson, A. I. Congenital urethral polyp in a child, 278
Bailey, R. R., jt. author. *See* Tremewan, R. N.
Ball, S. G., Giles, G. R., McLachlan, M. S. F. and Lee, M. R. Autotransplantation of the kidney for fibromuscular dysplasia of the renal arteries, 227
Baltopoulos, G., jt. author. *See* Delides, G. S.
Bapna, B. C., jt. author. *See* Sharma, S. K.
Ben-Bassat, M., jt. author. *See* Fischelovitch, J.
Bentley, P. G. and Higgs, D. R. Peritoneal tuberculosis with ureteric obstruction, mimicking retroperitoneal fibrosis, 170
Berni, G., jt. author. *See* Selli, C.
Bhat, H. S., jt. author. *See* Sasidharan, K.
Blandy, J. P. and Marshall, V. R. Size of renal calculi, recurrence rate and follow-up, 525
Blandy, J. P., Wadhwa, S., Singh, M. and Tresidder, G. C. Urethroplasty in context, 697
Blandy, J. P., jt. author. *See* Molland, E. A.
Blath, R. A. and Bucy, J. G. Localised primary amyloidosis of the bladder, 219
Bloom, H. J. G., jt. author. *See* Wallace, D. M.
Boardman, K. P. Duodenal and common bile duct obstruction with a pyelo-duodenal fistula caused by renal calculous pyonephrosis, 6
Bourne, R., jt. author. *See* Hoyes, A. D.
Bowyer, R. C., jt. author. *See* Thalut, K.
Boyd, P. J. R., jt. author. *See* Burnand, K. G.
Bradley, W. E., jt. author. *See* Andersen, J. T.
Bradley, W. E., jt. author. *See* Jensen, J. T.
Briscoe, C. E., jt. author. *See* Doyle, P. T.
Brockis, J. G., jt. author. *See* Thalut, K.
Bruce, A. W., jt. author. *See* Seddon, J. M.
Brumfitt, W., jt. author. *See* Hardy, J. D.
Bryson, J. R., jt. author. *See* Smith, P. J. B.
Bucy, J. G., jt. author. *See* Blath, R. A.
Bultitude, M. I., Hills, N. H. and Shuttleworth, K. E. D. Clinical and experimental studies on the action of prostaglandins and their synthesis inhibitors on detrusor muscle *in vitro* and *in vivo*, 631
Burnand, K. G., Boyd, P. J. R., Mayo, M. E., Shuttleworth, K. E. D. and Lloyd-Davies, R. W. Single dose intravesical thiotepa as an adjuvant to cystodiathermy in the treatment of transitional cell bladder carcinoma, 55
Bye, A., jt. author. *See* Dabhoiwala, N. F.
Byrd, R. B., Viner, N. A., Omell, G. H. and Trunk, G. Leukoplakia associated with renal tuberculosis in the chemotherapeutic era, 377
Byrne, P. O., jt. author. *See* Hall, R. R.

Caine, M., Pfau, A. and Perlberg, S. The use of alpha-adrenergic blockers in benign prostatic obstruction, 255
Cameron, K. M. and Lupton, C. H. Inverted papillomas of the lower urinary tract, 567
Cameron, K. M., jt. author. *See* Pryor, J. P.
Campbell, I. W., jt. author. *See* Fraser, D. M.
Carswell, G. F. A case of Behçet's disease involving the bladder, 199
Carter, D., jt. author. *See* Seddon, J. M.
Castro, J. E., jt. author. *See* Osborn, D. E.
Castro, J. E., jt. author. *See* Sinha, S. N.
Castro, J. E., jt. author. *See* Williams, G.
Chabra, J. S., jt. author. *See* Sharma, S. K.
Chadwick, P., jt. author. *See* Seddon, J. M.
Chisholm, G. D., jt. author. *See* O'Donoghue, E. P. N.
Claridge, M., jt. author. *See* Dabhoiwala, N. F.
Clark, P. and Hosmane, R. U. Re-implantation of the ureter, 31
Clark, P. B., jt. author. *See* Vijayan, P.
Cohanim, M., jt. author. *See* Yendt, E. R.
Collins, W. P , jt. author. *See* Pryor, J. P.
Condon, J. R., Milsted, R. A. V. and Nassim, J. R. Hyperparathyroidism and sodium cellulose phosphate, 316
Cook, J. B. and Smith, P. H. Percutaneous suprapubic cystostomy after spinal cord injury, 119
Cortivo, R., jt. author. *See* Pagano, F.
Craggs, M. D. and Stephenson, J. D. The real bladder electromyogram, 443
Crisp, J. C. Random bone marrow biopsy in the staging of carcinoma of the prostate, 265
Crisp, J. C., Green, N. A. and Ashken, M. H. Urodynamic studies in the District General Hospital, 383
Cross, R. J., Glashan, R. W., Humphrey, C. S., Robinson, M. R. G., Smith, P. H. and Williams, R. E. Treatment of advanced bladder cancer with adriamycin and 5-fluorouracil, 609

Dabhoiwala, N. F., Bye, A. and Claridge, M. A study of concentrations of trimethoprim-sulphamethoxazole in the human prostate gland, 77
Daga-Gordini, D., jt. author. *See* Pagano, F.
Davidson, A. I., jt. author. *See* Bagley, F. H.

48/7—o

Davies, J. M., Somerville, S. M. and Wallace, D. M. Occupational bladder tumour cases identified during ten years' interviewing of patients, 561
Dawson-Edwards, P., jt. author. *See* Hughes, M. A.
Dekeyser, W., jt. author. *See* Popelier, G.
Delides, G. S., Baltopoulos, G. and Papaharalampous, N. X. Latent carcinoma of the prostate: the probability of identifying small lesions in routine histology, 207
Dhayagude, H. C., jt. author. *See* Tilak, G. H.
Di Paola, M. and Stockwell, W. S. Appendicovesical fistula due to an appendix abscess with associated goblet cell carcinoid of the appendix, 436
Dick, A., jt. author. *See* Whyte, A. S.
Downie, J. W., jt. author. *See* Awad, S. A.
Doyle, P. T. and Briscoe, C. E. The effects of drugs and anaesthetic agents on the urinary bladder and sphincters, 329
Duff, F. A., jt. author. *See* Narayana, A. S.
Dunn, M., jt. author. *See* Ramsden, P. D.

Eeckhout, E. van den, jt. author. *See* Popelier, G.
Evans, D. H., jt. author. *See* Rider, W. D.
Evans, P. R., jt. author. *See* Usherwood, M. McD.
Evans, P. R. jt. author. *See* Yu H. Y. H.

Fair, W. R. and Govan, D. E. Influence of vesicoureteral reflux on the response to treatment of urinary tract infections in female children, 111
Farkas, A. and Skinner, D. G. Posterior urethral valves in siblings, 76
Farrar, D. J. and Osborne, J. L. The use of bromocriptine in the treatment of the unstable bladder, 235
Farrar, D. J. and Pryor, J. S. The effect of bromocriptine in patients with benign prostatic hypertrophy, 73
Feggetter, J. G. W. An osteolytic lesion as a presentation of bladder carcinoma, 254
Feldman, R. A., jt. author. *See* Schiff, M.
Feneley, R. C. L., jt. author. *See* Abrams, P. H.
Fine, H. and Keen, E. N. Some observations on the medulla of the kidney, 161
Fischelovitch, J. and Avidor, I. Leukoplakia of renal pelvis, 376
Fischelovitch, J. and Ben-Bassat, M. Female hypospadias, 72
Fischelovitch, J., jt. author. *See* Traub, Y. M.
Foote, J. W., jt. author. *See* Schwarz, R. D.
Franks, A. J., jt. author. *See* Fraser, D. M.
Fraser, D. M., Franks, A. J. and Campbell, I. W. Reversible neuromyopathy in hypernephroma, 340
Fujita, H., jt. author. *See* Shimada, K.
Furnell, P. M., jt. author. *See* Hardy, J. D.

Gallagher, B. L. S. and Hashmat, A. I. Malignant testicular lymphoma in brothers, 210
Gallagher, F., jt. author. *See* Narayana, A. S.
Galli, E. M., jt. author. *See* O'Boyle, P. J.
Garousche, A. R., jt. author. *See* Smith, P.
Geddes, J. R., jt. author. *See* Hughes, M. A.
Gibbon, N. O. K., jt. author. *See* O'Boyle, P. J.
Gibbon, N. O. K., jt. author. *See* Ross, J. C.
Giles, G. R., jt. author. *See* Ball, S. G.
Gingell, J. C., jt. author. *See* Osborne, D.
Glashan, R. W., jt. author. *See* Cross, R. J.
Golovsky, D., jt. author. *See* Morris, M. J.
Govan, D. E., jt. author. *See* Fair, W. R.
Gow, J. G., jt. author. *See* O'Boyle, P. J.
Gow, J. G., jt. author. *See* Tidd, M. J.
Green, N. A., jt. author. *See* Crisp, J. C.
Griffiths, D. A. A reappraisal of the Pfannenstiel incision, 469
Guinness, M. D. G., jt. author. *See* Morris, M. J.
Gupta, I. M., jt. author. *See* Gupta, S.
Gupta, K. G., jt. author. *See* Jenkins, D. G.
Gupta, S. and Gupta, I. M. Ectopia vesicae complicated by squamous cell carcinoma, 244

Halim, A., jt. author. *See* Usherwood, M. McD.
Halim, A., jt. author. *See* Yu, H. Y. H.
Hall, R. R., Wadehra, V., Towler, J. M., Hindmarsh, J. R. and Byrne, P. O. Hyperthermia in the treatment of bladder tumours, 603
Hallson, P. C. and Rose, G. A. Crystalluria in normal subjects and in stone formers with and without thiazide and cellulose phosphate treatment, 515
Hammonds, J. C., Williams, J. L. and Harvey, L. Primary hyperparathyroidism—a review of cases in the Sheffield area, 539
Hardy, J. D., Furnell, P. M. and Brumfitt, W. Comparison of sterile bag, clean catch and suprapubic aspiration in the diagnosis of urinary infection in early childhood, 279
Harper, W. E. S. and Matz, L. R. Further studies on effects of irrigation solutions on rat bladders, 463
Harrison, N. W., jt. author. *See* Snyder, H. M.
Harrison, N. W., jt. author. *See* Whitfield, H. N.
Harvey, L., jt. author. *See* Hammonds, J. C.
Hashmat, A. I., jt. author. *See* Gallagher, B. L. S.
Hendry, W. F., jt. author. *See* Serrao, A.
Hendry, W. F., jt. author. *See* Turner, A. G.
Higgs, D. R., jt. author. *See* Bentley, P. G.
Hiles, R. W., jt. author. *See* Smith, P. J. B.
Hills, N. H., jt. author. *See* Bultitude, M. I.
Hindmarsh, J. R., jt. author. *See* Hall, R. R.
Hodgkinson, A. Uric acid disorders in patients with calcium stones, 1
Hosmane, R. U., jt. author. *See* Clark, P.
Hoyes, A. D., Bourne, R. and Martin, B. G. H. Innervation of the muscle of the bladder in the rat, 43
Hughes, M. A., Arkell, D. G., Dawson-Edwards, P. and Geddes, J. R. Contralateral ureteric metastasis from renal carcinoma, 402
Humphrey, C. S., jt. author. *See* Cross, R. J.

International Continence Society. First report on the standardisation of terminology of lower urinary tract function, 39
Ipiéns Aznar, A. and Martinez-Peñuela V., J. M. Urinary retention due to congenital posterior urethral polyp in a boy, 478

Jackaman, F. R. Recurrent spontaneous rupture of the urinary bladder, 54
Jameson, R. M. Regression of penile metastases of prostatic carcinoma with cyproterone acetate therapy, 268
Jenkins, D. G. and Gupta, K. G. Complete avulsion of the renal pedicle due to blunt injury to abdomen, 12
Jequier, A. M. Urinary symptoms and total hysterectomy, 437

Jewett, M. A. S., jt. author. *See* Romans, D. G.
Johnston, J. H. and Mix, L. W. The Ask-Upmark kidney: a form of ascending pyelonephritis?, 393
Johnston, J. H., Shapiro, S. R. and Thomas, G. G. Anti-reflux surgery in the congenital neuropathic bladder, 639
Jones, P. A., jt. author. *See* Serrao, A.
Joshi, S. S., jt. author. *See* Tilak, G. H.

Katsumi, T., jt. author. *See* Shimada, K.
Keen, E. N., jt. author. *See* Fine, H.
Kelly, D. G., jt. author. *See* Narayana, A. S.
Kenawi, M. M. and Williams, D. Innes. Circumcaval ureter: a report of four cases in children with a review of the literature and a new classification, 183
Kettlewell, M. G., jt. author. *See* Smith, R. B.
Koff, S. A., jt. author. *See* Vinson, R. K.
Kupelian, S. and Robinson, M. R. G. Pelvic lipomatosis presenting as acute ureteric obstruction, 389

Laurenti, C., jt. author. *See* Tacciuoli, M.
Lee, M. R., jt. author. *See* Ball S. G.
Leong, C. H., Wong, K. K. and Saw, D. Asymptomatic phaeochromocytoma of the bladder coexisting with carcinoma, 123
Little, P. J., jt. author. *See* Tremewan, R. N.
Lloyd-Davies, R. W., jt. author. *See* Burnand, K. G.
Lubin, E., jt. author. *See* Traub, Y. M.
Luck, R. J., jt. author. *See* Salem, R. J.
Ludgate, C. M. and Watson, G. S. Unilateral renal hypertension following major trauma, 362
Lupton, C. H., jt. author. *See* Cameron, K. M.

McCredie, D. A., Powell, H. R. and Rotenberg, E. Diphosphonate therapy in nephrocalcinosis, 93
Macdonald, J. S., jt. author. *See* Turner, A. G.
McGeown, M. G., jt. author. *See* Welshman, S. G.
Mackinnon, K. J., jt. author. *See* Schwarz, R. D.
McLachlan, M. S. F., jt author. *See* Ball, S. G.
McLoughlin, M. G. Ureterocalyostomy, 328
Magri, J., jt. author. *See* Stuart, A. E.
Maher, P. O., jt. author. *See* Morris, M. J.
Maling, T. M. J., jt. author. *See* Tremewan, R. N.
Mallik, M. K., jt. author. *See* Serrao, A.
Marshall, V. R., jt. author. *See* Blandy J. P.
Martin B. G. H. jt. author. *See* Hoyes A. D.
Martinez-Peñuela V., J. M. jt. author. *See* Ipiéns Aznar, A.
Matz, L. R., jt. author. *See* Harper, W. E. S.
Mayo, M. E., jt. author. *See* Burnand, K. G.
Milsted, R. A. V., jt. author. *See* Condon, J. R.
Mix, L. W., jt. author. *See* Johnston, J. H.
Molland, E. A., Trott, P. A., Paris, A. M. I. and Blandy, J. P. Nephrogenic adenoma: a form of adenomatous metaplasia of the bladder. A clinical and electron microscopical study, 453
Monga, L. S. An apparatus for Helmstein's hydrostatic pressure treatment, 311
Moores, W. K. The surgical significance of the proteus stone, 399
Morehouse, D. D., jt. author. *See* Schwarz, R. D.
Morris, M. J., Golovsky, D., Guinness, M. D. G. and Maher, P. O. The value of prophylactic antibiotics in transurethral prostatic resection: a controlled trial, with observations on the origin of postoperative infection, 479

Mysorekar, V. R. Accessory vas deferens: a case report, 82

Nair, V. R. Vasoplasty: a new technique, 269
Narayana, A. S., Gallagher, F., Kelly, D. G. and Duff, F. A. Hydronephrosis and polycythaemia, 175
Narayana, A. S., Kelly, D. G. and Duff, F. A. Tuberculosis of the penis, 274
Nassim, J. R., jt. author. *See* Condon, J. R.
Nathan, H., Tobias, P. V. and Wellsted, M. D. An unusual case of right and left testicular arteries arching over the left renal vein, 135
Neri, A., jt. author. *See* Traub, Y. M.
Newill, R. A.I.D.—a review of 200 cases, 139
Newton, J. R., jt. author. *See* Pryor, J. P.

O'Boyle, P. J., Galli, E. M. and Gow, J. G. The surgical management of tuberculous lower ureteric stricture, 101
O'Boyle, P. J. and Gibbon, N. O. K. Vaginal ureterolithotomy, 231
O'Donoghue, E. P. N., Shridhar, P., Sherwood, T., Williams, J. P. and Chisholm, G. D. Lymphography and pelvic lymphadenectomy in carcinoma of the prostate, 689
O'Flynn, J. D. An assessment of surgical treatment of vesical outlet obstruction in spinal cord injury: a review of 471 cases, 657
Omell, G. H., jt. author. *See* Byrd, R. B.
Oosterlinck, W. and Renders, G. A knot in the urethra, 284
Orestano, F. and Altwein, J. E. Testosterone metabolism in benign prostatic hypertrophy: *in vivo* studies of gestonorone caproate and cyproterone acetate, 485
Osborn, D. E., Castro, J. E., and Shackman, R. Surgical correction of arterial stenosis in renal allografts, 221
Osborne, D. and Gingell, J. C. Posterior urethral duplication, 264
Osborne, J. L., jt. author. *See* Farrar, D. J.

Pagano, F., Passerini, G., Cortivo, R., Daga-Gordini, D., and Abatangelo, G. The elastic component of normal and dilated ureters in children: chemical and histochemical characterisation, 13
Paola, M. di. *See* di Paola, M.
Papaharalampous, N. X., jt. author. *See* Delides, G. S.
Paris, A. M. I., jt. author. *See* Molland, E. A.
Passerini, G., jt. author. *See* Pagano, F.
Pearman, J. W. Urological follow-up of 99 spinal cord injured patients initially managed by intermittent catheterisation, 297
Peckham, M. J., jt. author. *See* Tyrrell, C. J.
Pennington, J. H., jt. author. *See* Todd, M. J.
Perlberg, S., jt. author. *See* Caine, M.
Peters, T. M., jt. author. *See* Tremewan, R. N.
Pfau, A. and Sacks, T. Chronic bacterial prostatitis: new therapeutic aspects, 245
Pfau, A., jt. author. *See* Caine, M.
Popelier, G., Eeckhout, E. van den and Dekeyser, W. Composition of bladder stones in Rwanda, 317
Powell, H. R., jt. author. *See* McCredie, D. A.
Prasad, S. Filariasis penis, 426

Pryor, J. P., Pugh, R. C. B., Cameron, K. M., Newton, J. R. and Collins, W. P. Plasma gonadotrophic hormones, testicular biopsy and seminal analysis in the men of infertile marriages, 709
Pryor, J. S., jt. author. *See* Farrar, D. J.
Pugh, R. C. B., jt. author. *See* Pryor, J. P.

Quartey, J. K. M., jt. author. *See* Ribeiro, F.

Racheli, T., jt. author. *See* Tacciuoli, M.
Ramsden, P. D., Smith, J. C., Dunn, M. and Ardran, G. M. Distension therapy for the unstable bladder: later results including an assessment of repeat distensions, 623
Rao, M. M., jt. author. *See* Sasidharan, K.
Renders, G., jt. author. *See* Oosterlinck, W.
Ribeiro, F. and Quartey, J. K. M. Traumatic avulsion of the ureter with obstruction, pseudocyst formation and hypertension, 107
Rider, W. D. and Evans, D. H Radiotherapy in the treatment of recurrent bladder cancer, 595
Rizal, A , jt. author. *See* Thalut, K.
Roberts, M., jt. author. *See* Smith, P.
Robinson, M. R. G., jt. author. *See* Cross, R. J.
Robinson, M. R. G., jt. author. *See* Kupelian, S.
Robson, C. J., jt. author. *See* Romans, D. G.
Romans, D. G., Jewett, M. A. S. and Robson, C. J. Crossed renal ectopia with colic: a clinical clue to embryogenesis, 171
Rose, G. A. Studies on the chemical nature of urinary chemiluminescence, 61
Rose, G. A. and Woodfine, C. The thermogravimetric analysis of renal stones (in clinical practice), 403
Rose, G. A., jt. author. *See* Hallson, P. C.
Rosen, M. A simple artificial implantable sphincter, 675
Ross, R. C., Gibbon, N. O. K. and Sundar, G. S. Division of the external urethral sphincter in the neuropathic bladder: a twenty years' review, 649
Rotenberg, E., jt. author. *See* McCredie, D. A.
Roylance, J , jt. author. *See* Abrams, P. H.
Royle, G. and Smith, J. C. Recurrence of infected calculi following postoperative renal irrigation with stone solvent, 531

Sacks, T., jt. author. *See* Pfau, A.
Salem, R. J. and Luck, R. J. Midline ensheathed ureters, 18
Sasidharan, K., Babu, A. S., Rao, M. M. and Bhat, H. S. Free supernumerary kidney, 388
Saw, D., jt. author. *See* Leong, C. H.
Schiff, M. and Feldman, R. A. Lymphocele following renal transplantation: an unusual cause of urinary retention, 122
Schwarz, R. D., Foote, J. W., Morehouse, D. D., and Mackinnon, K. J. The assessment of sphincteric activity in patients following transsphincteric urethral reconstruction, 643
Scott, M. R., jt. author. *See* Tidd, M. J.
Seddon, J M., Bruce A. W., Chadwick P. and Carter, D. Introital bacterial flora—effect of increased frequency of micturition, 211
Selli, C., Turini, D. and Berni, G. Embolism in a single functioning kidney: report of two cases, 419
Serrao, A., Mallik, M. L., Jones, P. A., Hendry, W. F. and Wickham, J. E. A. Hypothermic prostatic resection, 685
Shackman, R., jt. author. *See* Osborn, D. E.
Shapiro, S. R., jt. author. *See* Johnston, J. H.
Sharma, S. K., Bapna, B. C. and Singh, S. M. Familial profile of transitional cell carcinoma, 442
Sharma, S. K., Wadhwa, S. N. and Chabra, J. S. Primary vaginal stone, 336
Shelton, J., jt. author. *See* Tidd, M. J.
Sherwood, T., jt. author. *See* O'Donoghue, E. P. N.
Sherwood, T., jt. author. *See* Whitfield, H. N.
Shimada, K., Katsumi, T. and Fujita, H. Appendiceal granuloma causing bilateral hydronephrosis and macroscopic haematuria, 418
Shridhar, P., jt. author. *See* O'Donoghue, E. P. N.
Shuttleworth, K. E. D., jt. author. *See* Bultitude, M. I.
Shuttleworth, K. E. D., jt. author. *See* Burnand, K. G.
Silverton, N. P. Testicular metastasis from prostatic carcinoma, 498
Singh, M., jt. author. *See* Blandy, J. P.
Singh, S. M., jt. author. *See* Sharma, S. K.
Sinha, S. N. and Castro, J. E. Allograft nephrectomy, 413
Skinner, D. G., jt. author. *See* Farkas, A.
Smith, J. C., jt. author. *See* Ramsden, P. D.
Smith, J. C., jt. author. *See* Royle, G.
Smith, P., Roberts, M., Whitaker, R. H. and Garousche, A. R. Primary pelvic hydronephrosis in children: a retrospective survey, 549
Smith, P. H., jt. author. *See* Cook, J. B.
Smith, P. H., jt. author. *See* Cross, R. J.
Smith, P. J. B., Townsend, P. L. G., Hiles, R. W. and Bryson, J. R. Hypospadias—problems of postoperative fistulae formation and a modified 2-stage procedure to reduce these, 703
Smith, R. B. and Kettlewell, M. G. Rupture of a bladder diverticulum in multiple sclerosis, 382
Snyder, H. M., Harrison, N. W., Whitfield, H. N. and Williams, D. I. Urodynamics in the prune belly syndrome, 663
Snyder, H. M., jt. author. *See* Williams, D. Innes
Somerville, S. M., jt. author. *See* Davies, J. M.
Stephenson, J. D., jt. author. *See* Craggs, M. D.
Stief, K., jt. author. *See* Zingg, E.
Stockwell, W. S., jt. author. *See* Di Paola, M.
Stuart, A. E. and Magri, J. Long survival after vaginal sarcoma botryoides, 452
Sutor, D. J. A simple method for studying the formation of calcium oxalate, 177

Tacciuoli, M., Laurenti, C. and Racheli, T. Trigonal cysts in childhood, 323
Tait, J. J., jt. author. *See* Tremewan, R. N.
Takayasu, H., jt. author. *See* Terada Y.
Tanagho E. A. Male epispadias: surgical repairs of urethropenile deformity 127
Taylor T. A. jt. author. *See* Thalut, K.
Terada, Y. and Takayasu, H. Malignant melanoma of the male urethra, 390
Tettamanti, F., jt. author. *See* Tscholl, R.
Thalut, K., Rizal, A., Brockis, J. G., Bowyer, R. C., Taylor, T. A. and Wisniewski, Z. S. The endemic bladder stones of Indonesia—epidemiology and clinical features, 617
Thomas, G. G., jt. author. *See* Johnston, J. H.
Thomas, J. A. and Antony, A. J. Amoebiasis of the penis, 269

Tidd, M. J., Gow, J. G., Pennington, J. H., Shelton, J. and Scott M. R. Comparison of hydrophilic polymer-coated latex, uncoated latex and PVC indwelling balloon catheters in the prevention of urinary infection 285

Tilak G. H. Dhayagude H. C. and Joshi S. S. Badenoch's pull-through operation for urethral stricture 83

Tobias P. V., jt. author. *See* Nathan, H.

Towler, J. M., jt. author. *See* Hall, R. R.

Townsend, P. L. G., jt. author. *See* Smith, P. J. B.

Traub, Y. M., Fischelovitch, J. M., Neri, A. and Lubin, E. Endometriosis mimicking ureterolithiasis, 27

Tremewan, R. N., Bailey, R. R., Little, P. J., Maling, T. M. J., Peters, T. M. and Tait, J. J. Diagnosis of gross vesico-ureteric reflux using ultrasonography, 431

Tresidder, G. C., jt. author. *See* Blandy, J. P.

Trott, P. A., jt. author. *See* Molland, E. A.

Trunk, G., jt. author. *See* Byrd, R. B.

Tscholl, R., Tettamanti, F. and Worsdorfer, O. The urethral pressure profile recorded by means of CO_2-perfusion at high flow rates, 337

Tscholl, R., jt. author. *See* Zingg, E.

Turini, D., jt. author. *See* Selli, C.

Turner, A. G., Hendry, W. F., Macdonald, J. S. and Wallace, D. M. The value of lymphography in the management of bladder cancer, 579

Tyrrell, C. J. and Peckham, M. J. The response of lymph node metastases of testicular teratoma to radiation therapy, 363

Usherwood, M. McD., Halim, A. and Evans, P. R. Artificial insemination (A.I.H.) for sperm antibodies and oligozoospermia, 499

Vijayan, P., Clark, P. B. and Anderson, C. K. Leukoplakia of the male urethra, 346

Viner, N. A., jt. author. *See* Byrd, R. B.

Vinson, R. K. and Koff, S. A. Obstructing prostatic urethral calculi, 492

Wadehra, V., jt. author. *See* Hall, R. R.

Wadhwa, S. jt. author. *See* Blandy, J. P.

Wadhwa S. N. jt. author. *See* Sharma, S. K.

Wallace, D. M. and Bloom, H. J. G. The management of deeply infiltrating (T_3) bladder carcinoma: controlled trial of radical radiotherapy versus preoperative radiotherapy and radical cystectomy (first report), 587

Wallace, D. M., jt. author. *See* Davies, J. M.

Wallace, D. M., jt. author. *See* Turner, A. G.

Watson, G. S., jt. author. *See* Ludgate, C. M.

Way, S. and Young, J. R. Ureteric invasion by endometriosis, 38

Weinberg, R. W. Appendix ureteroplasty, 234

Wellsted, M. D., jt. author. *See* Nathan, H.

Welshman, S. G. and McGeown, M. G. Urinary citrate excretion in stone-formers and normal controls, 7

Wesolowski, S. Bilateral renal carcinomas treated operatively, 118

Wesolowski, S. Ileal replacement of ureter of solitary kidney: 22-year follow-up, 292

Whitaker, R. H. Reflux induced pelvic-ureteric obstruction, 555

Whitaker, R. H., jt. author. *See* Smith, P.

Whitfield, H. N., Harrison, N. W., Sherwood, T. and Williams, D. Innes. Upper urinary tract obstruction: pressure/flow studies in children, 427

Whitfield, H. N., jt. author. *See* Snyder, H. M.

Whyte, A. S. and Dick, A. A gynaecological presentation of phaeochromocytoma of the urinary bladder, 468

Wickham, J. E. A., jt. author. *See* Serrao, A.

Williams, D. Innes and Snyder, H. M. Anterior detrusor tube repair for urinary incontinence in children, 671

Williams, D. Innes, jt. author. *See* Kenawi, M. M.

Williams, D. Innes, jt. author. *See* Snyder, H. M.

Williams, D. Innes, jt. author. *See* Whitfield, H. N.

Williams, G. and Castro, J. E. A complication of nephrectomy by the supracostal approach, 106

Williams, J. L., jt. author. *See* Hammonds, J. C.

Williams, J. P., jt. author. *See* O'Donoghue, E. P. N.

Williams, R. E., jt. author. *See* Cross, R. J.

Wisniewski, Z. S., jt. author. *See* Thalut, K.

Wong, K. K., jt. author. *See* Leong, C. H.

Woodfine, C., jt. author. *See* Rose, G. A.

Worsdorfer, O., jt. author. *See* Tscholl, R.

Wright, B. M. Cryosurgery for prostatic obstruction using liquid nitrous oxide: preliminary communication, 203

Yendt, E. R. and Cohanim, M. The management of the patient with calcium stones, 507

Young, J. R., jt. author *See* Way, S.

Yu, H. Y. H., Halim, A. and Evans, P. R. Chlorhexidine for irrigation of vas: a clinical trial and the study of viability of non-motile sperms in post-vasectomy patients with trypan blue uptake, 371

Zingg, E., Tscholl, T. and Stief, K. Live television transmission of transurethral and open pelvic surgery with reproduction on a big screen, 475

SUBJECT INDEX

A.I.D., review of 200 cases, 139
A.I.H. for sperm antibodies and oligozoospermia, 499
Abdomen, blunt injury to, causing complete avulsion of the renal pedicle, 12
ABSTRACTS FROM CURRENT UROLOGICAL LITERATURE, 296, 595
Adenoma, nephrogenic, 453
Adriamycin and 5-fluorouracil in treatment of advanced bladder cancer, 609
Allograft nephrectomy, 413
Alpha-adrenergic blockers, use in benign prostatic obstruction, 255
Amoebiasis of the penis, 269
Amyloidosis, localised primary, of the bladder, 219
Anaesthetic agents, effects on urinary bladder and sphincters, 329
Analysis, thermogravimetric, of renal stones, 403
Antibiotics, prophylactic, in transurethral prostatic resection, 479
Appendico-vesical fistula due to appendix abscess with associated goblet cell carcinoid of appendix, 436
Appendix—
  abscess, with goblet cell carcinoid, causing appendico-vesical fistula, 436
  goblet cell cardinoid, associated with appendix abscess, and appendico-vesical fistula, 436
Appendix ureteroplasty, 234
Arteries, testicular, arching over the left renal vein, 135
Artificial insemination (A.I.H.) for sperm antibodies and oligozoospermia, 499

Badenoch's pull-through operation for urethral stricture, 83
Behçet's disease involving the bladder, 199
Bladder—
  adenomatous metaplasia of, 453
  and Behçet's disease, 199
  asymptomatic phaeochromocytoma co-existing with carcinoma, 123
  cancer, advanced, treatment with adriamycin and 5-flourouracil, 609
    lymphography in management of, 579
    recurrent, radiotherapy in treatment of, 595
  carcinoma, presenting as an osteolytic lesion, 254
    radical radiotherapy *v.* preoperative radiotherapy and radical cystectomy, 587
    transitional cell, treated by single dose intravesical thiotepa as an adjuvant to cystodiathermy, 55
  congenital neuropathic, anti-reflux surgery, 639
  diverticulum, rupture of, in multiple sclerosis, 382
  electromyogram, real, 443
  innervation in multiple sclerosis, 239
  localised primary amyloidosis of, 219
  muscle, innervation of, in the rat, 43
  neuropathic, division of external urethral sphincter in, 649
  rat, effects of irrigation solutions, 463
  stones, endemic, of Indonesia, 617
  stones, in Rwanda, composition of, 317
  tumour, occupational, cases identified, 561
  tumours, hyperthermia in treatment of, 603
  unstable, bromocriptine in treatment of, 235
    distension therapy for, 623
  urinary, phaeochromocytoma, gynaecological presentation, 468
    recurrent spontaneous rupture of, 54
Bone marrow biopsy, random, in staging of carcinoma of the prostate, 265
BOOK REVIEWS—
  ANDERSON, R. J., GAMBERTOGLIO, J. G. and SCHRIER, R. W., *Clinical use of drugs in renal failure*, 1975, 391
  BECKER, E. L. *ed.*, *Cornell Seminars on Nephrology*, 1973, 89
  BODNER, H., *Diagnostic and therapeutic aids in urology*, 1974, 89
  BROCKLEHURST, G. *ed.*, *Spina bifida for the clinician*, 1976, 391
  CORNIL, C., *Urethral obstruction in boys. Diagnosis and treatment of congenital valve of the posterior urethra*, 1975, 157
  DRESSER, D. W. *ed.*, *Immunological tolerance. British Medical Bulletin*, vol. 32, no. 2, 1976, 504
  GOLAND, M. *ed.*, *Normal and abnormal growth of the prostate*, 1975, 158
  HOLDEN, H. B., *ed.*, *Practical cryosurgery*, 1976, 293
  KINCAID-SMITH, P. *The kidney—a clinico-pathological study*, 1976, 293
  MOORHEAD, J. F. *ed.—Dialysis, transplantation, nephrology*. (Proceedings of the European Dialysis and Transplant Association, vol. 11) 1975, 89
  MURPHY, G. P. and MITTELMAN, A. *eds.*, *Chemotherapy of urogenital tumours*, 1975, 293
  RAYNAUD, C. *ed.*, *The renal uptake of radioactive mercury* ($^{197}HgCl_2$), 1975, 392
  REUTER, G. J. *ed.*, *Cryosurgery in urology: International Symposium in Stuttgart, 1973*, 1974, 392
  STRAUSS, J. *ed.*, *Pediatric nephrology*. Vol. 1, 1974, 157
  SUKI, W. N. and EKNOYAN, G. *eds.*, *The kidney in systemic disease*, 1976, 391
BOOKS RECEIVED—
  Advances in voluntary sterilisation. Proceedings of the 2nd International Conference, Geneva 1973. Ed. M. E. SCHIMA, 1974, 158
  BAZZATO, G. and ONESTI, G., *Hemodialysis in the home*, 1975, 90
  ECKERT, C. *ed.*, *Emergency room care*, 3rd ed., 1976, 392
  FREE, A. and FREE, H. M., *Urinalysis in clinical laboratory practice*, 1976, 392
BRITISH ASSOCIATION FOR PAEDIATRIC NEPHROLOGY, Spring meeting, 1976: announcement, 159
BRITISH ASSOCIATION OF UROLOGICAL SURGEONS—
  Annual meeting 1976: Programme, 158
  32nd Annual Meeting, 1976. Papers presented:
    Abrams, P. H., Roylance, J. and Feneley, R. C. L. Excretion urography in the investigation of prostatism, 681
    Blandy, J. P. and Marshall, V. R. Size of renal calculi, recurrence rate and follow-up, 525
    Blandy, J. P., Wadhwa, S., Singh, M. and Tresidder, G. C. Urethroplasty in context, 697

- BRITISH ASSOCIATION OF UROLOGICAL SURGEONS—
  - Annual meeting 1976. Papers presented:
    - Bultitude, M. I., Hills, N. H. and Shuttleworth, K. E. D. Clinical and experimental studies on the action of prostaglandins and their synthesis inhibitors on detrusor muscle *in vitro* and *in vivo*, 631
    - Cameron, K. M. and Lupton, C. H. Inverted papillomas of the lower urinary tract, 567
    - Cross, R. J., Glashan, R. W., Humphrey, C. S., Robinson, M. R. G., Smith, P. H. and Williams, R. E. Treatment of advanced bladder cancer with adriamycin and 5-flourouracil, 609
    - Davies, J. M., Somerville, S. M. and Wallace, D. M. Occupational bladder tumour cases identified during ten years' interviewing of patients, 561
    - Hall, R. R., Wadehra, V., Towler, J. M., Hindmarsh, J. R. and Byrne, P. O. Hyperthermia in the treatment of bladder tumours, 603
    - Hallson, P. C. and Rose, G. A. Crystalluria in normal subjects and in stone formers with and without thiazide and cellulose phosphate treatment, 515
    - Hammonds, J. C., Williams, J. L. and Harvey, L. Primary hyperparathyroidism—a review of cases in the Sheffield area, 539
    - Johnston, J. H., Shapiro, S. R. and Thomas, G. G. Anti-reflux surgery in the congenital neuropathic bladder, 639
    - O'Donoghue, E. P. N., Shridhar, P., Sherwood, T., Williams, J. P. and Chisholm, G. D. Lymphography and pelvic lymphadenectomy in carcinoma of the prostate, 689
    - O'Flynn, J. D. An assessment of surgical treatment of vesical outlet obstruction in spinal cord injury: a review of 471 cases, 657
    - Pryor, J. P., Pugh, R. C. B., Cameron, K. M., Newton, J. R. and Collins, W. P. Plasma gonadotrophic hormones, testicular biopsy and seminal analysis in the men of infertile marriages, 709
    - Ramsden, P. D., Smith, J. C., Dunn, M. and Ardran, G. M. Distension therapy for the unstable bladder: later results including an assessment of repeat distensions, 623
    - Rider, W. D. and Evans, D. H. Radiotherapy in the treatment of recurrent bladder cancer, 595
    - Rosen, M. A simple artificial implantable sphincter, 675
    - Ross, J. C., Gibbon, N. O. K. and Sundar, G. S. Division of the external urethral sphincter in the neuropathic bladder: a twenty years' review, 649
    - Royle, G. and Smith, J. C. Recurrence of infected calculi following postoperative renal irrigation with stone solvent, 531
    - Schwarz, R. D., Foote, J. W., Morehouse, D. D. and Mackinnon, K. J. The assessment of sphincteric activity in patients following transsphincteric urethral reconstruction, 643
    - Serrao, A., Mallik, M. K., Jones, P. A., Hendry, W. F. and Wickham, J. E. A. Hypothermic prostatic resection, 685
    - Smith, P., Roberts, M., Whitaker, R. H. and Garousche, A. R. Primary pelvic hydronephrosis in children: a retrospective survey, 549
    - Smith, P. J. B., Townsend, P. L. G., Hiles, R. W. and Bryson, J. R. Hypospadias—problems of postoperative fistulae formation and a modified 2-stage procedure to reduce these, 703
    - Snyder, H. M., Harrison, N. W., Whitfield, H. N. and Williams, D. Innes. Urodynamics in the prune belly syndrome, 663
    - Thalut, K., Rizal, A., Brockis, J. G., Bowyer, R. C., Taylor, T. A. and Wisniewski, Z. S. The endemic bladder stones of Indonesia—epidemiology and clinical features, 617
    - Turner, A. G., Hendry, W. F., Macdonald, J. S. and Wallace, D. M. The value of lymphography in the management of bladder cancer, 579
    - Wallace, D. M. and Bloom, H. J. G. The management of deeply infiltrating (T_3) bladder carcinoma: controlled trial of radical radiotherapy versus preoperative radiotherapy and radical cystectomy (first report), 587
    - Whitaker, R. H. Reflux induced pelvi-ureteric obstruction, 555
    - Williams, D. Innes and Snyder, H. M. Anterior detrusor tube repair for urinary incontinence in children, 671
    - Yendt, E. R. and Cohanim, M. The management of the patient with calcium stones, 507
- Bromocriptine—
  - effect in benign prostatic hypertrophy, 73
  - in treatment of the unstable bladder, 235

- Calcium oxalate formation, method of study, 177
- Calcium stone(s)—
  - and uric acid disorders, 1
  - management of patient, 507
- Calculus (i)—
  - infected, recurrence following postoperative renal irrigation with stone solvent, 531
  - prostatic urethral, 492
  - renal, size, recurrence rate and follow-up, 525
- Cancer—
  - bladder, advanced, treatment with adriamycin and 5-fluorouracil, 609
  - bladder, lymphography in management of, 579
  - bladder, recurrent, radiotherapy in treatment of, 595
  - prostatic, serum antibody in, 355
- Carcinoma(s)—
  - and asymptomatic phaeochromocytoma of the bladder, 123
  - bilateral renal, treated operatively, 118
  - bladder, deeply infiltrating, radical radiotherapy *v.* preoperative radiotherapy and radical cystectomy, 587
  - bladder, presenting as an osteolytic lesion, 254
  - latent, of prostate, 207
  - of prostate, random bone marrow biopsy in staging of, 265
  - prostate, lymphography and pelvic lymphadenectomy in, 689
  - prostatic, testicular metastasis from, 498
  - renal, contralateral ureteric metastasis from, 402
  - squamous cell, complicating ectopia vesicae, 244
  - transitional cell, familial profile, 442
  - transitional cell, of bladder, treated by thiotepa and cystodiathermy, 55
  - transitional cell, recurrent, complicating ileal conduit, 60

Catheter, PVC indwelling balloon, comparison with hydrophilic polymer-coated latex and uncoated latex in prevention of urinary infection, 285
Catheterisation, intermittent, spinal cord injured patients, managed by, 297
Cellulose phosphate treatment in stone formers, and crystalluria, 515
Chlorhexidine, for irrigation of vas, 371
Circumcaval ureter in children, 183
Clean catch, comparison with sterile bag and suprapubic aspiration in diagnosis of urinary infection in early childhood, 279
Composition of bladder stones in Rwanda, 317
Cryosurgery for prostatic obstruction using liquid nitrous oxide, 203
Crystalluria, in normal subjects and in stone formers, 515
Current urological literature, i, xix, xli
Cyproterone acetate, and testosterone metabolism in benign prostatic hypertrophy, 485
Cyproterone acetate therapy, in penile metastases of prostatic carcinoma, 268
Cysts, trigonal, in childhood, 323
Cystectomy, radical and preoperative radiotherapy *v.* radical radiotherapy in deeply infiltrating bladder carcinoma, 587
Cystostomy, percutaneous suprapubic, after spinal cord injury, 119

Detrusor dysfunction in prostatic hypertrophy, 493
Detrusor function, abnormalities, in multiple sclerosis, 193
Detrusor muscle, action of prostaglandins and their synthesis inhibitors on, 631
Diphosphonate therapy in nephrocalcinosis, 93
Distension therapy for the unstable bladder, 623
Drugs, effects on urinary bladder and sphincters, 329
Duodenal and common bile duct obstruction with a pyelo-duodenal fistula caused by renal calculous pyonephrosis, 6
Dysplasia, fibromuscular, of renal arteries, autotransplantation of the kidney for, 227

Ectopia, crossed renal, with colic, 171
Ectopia vesicae complicated by squamous cell carcinoma, 244
Electromyogram, bladder, real, 443
Embolism, in a single functioning kidney, 419
Endometriosis—
  mimicking ureterolithiasis, 27
  ureteric invasion by, 38
Epispadias, male, surgical repairs, 127
EUROPEAN ASSOCIATION OF UROLOGY, Prize essay contest: announcement, 90

Fibromuscular dysplasia of the renal arteries, autotransplantation of the kidney for, 227
Filariasis penis, 426
Fistula(e)—
  appendico-vesical, due to appendix abscess and associated goblet cell carcinoid, 436
  postoperative, in hypospadias, 703
  pyelo-duodenal, with duodenal and common bile duct obstruction, caused by renal calculous pyonephrosis, 6
5-fluorouracil and adriamycin in treatment of advanced bladder cancer, 609

Gestonorone caproate and testosterone metabolism in benign prostatic hypertrophy, 485
Goblet cell carcinoid of appendix, associated with appendix abscess, and appendico-vesical fistula, 436
Granuloma, appendiceal, causing bilateral hydronephrosis and macroscopic haematuria, 418

Haematuria, macroscopic, and bilateral hydronephrosis caused by appendiceal granuloma, 418
Helmstein's hydrostatic pressure treatment, apparatus for, 311
Hormones, plasma gonadotrophic, testicular biopsy and seminal analysis in men of infertile marriages, 709
Hydronephrosis—
  and polycythaemia, 175
  bilateral, and macroscopic haematuria, caused by appendiceal granuloma, 418
  primary pelvic, in children, 549
Hypernephroma with reversible neuromyopathy, 340
Hyperparathyroidism and sodium cellulose phosphate, 316
Hyperparathyroidism, primary, in Sheffield, 539
Hypertension and pseudocyst formation, in traumatic avulsion of the ureter, 107
Hyperthermia in treatment of bladder tumours, 603
Hypospadias—
  female, 72
  postoperative fistulae and 2-stage procedure to reduce them, 703
Hypothermic prostatic resection, 685
Hysterectomy, total, and urinary symptoms, 437

Ileal conduit complicated by recurrent transitional cell carcinoma, 60
Ileal ureter, experience with, 19
Incontinence, urinary, in children, anterior detrusor tube repair, 671
Indonesia, endemic bladder stones of, 617
Innervation of muscle of bladder in the rat, 43
INSTITUTE OF UROLOGY (UNIVERSITY OF LONDON)—
  Advance notice of meetings, September, November, December 1976, 295
  Announcement of courses, January-April 1977, 504
Introital bacterial flora, effect of increased frequency of micturition, 211
Irrigation solutions, effects on rat bladders, 463

Kidney—
  Ask-Upmark, form of ascending pyelonephritis?, 393
  autotransplantation, for fibromuscular dysplasia of the renal arteries, 227
  embolism in a single functioning, 419
  medulla of, 161
  solitary, ileal replacement of ureter of, 292
  supernumerary, free, 388
Knot in the urethra, 284

Latex—
  hydrophilic polymer-coated, comparison with uncoated latex and PVC indwelling balloon catheters in prevention of urinary infection, 285
  uncoated, comparison with hydrophilic polymer-coated latex and PVC indwelling balloon catheters in prevention of urinary infection, 285

Leukoplakia associated with renal tuberculosis, 377
Leukoplakia—
  of male urethra, 346
  of renal pelvis, 376
Lipomatosis, pelvic, presenting as acute ureteric obstruction, 389
Lymph node metastases, of testicular teratoma, response to radiation therapy, 363
Lymphadenectomy, pelvic, and lymphography in carcinoma of the prostate, 689
Lymphocele, following renal transplantation, causing urinary retention, 122
Lymphography—
  and pelvic lymphadenectomy in carcinoma of the prostate, 689
  in management of bladder cancer, 579
Lymphoma—
  testicular, malignant, in brothers, 210

Medulla of the kidney, 161
Melanoma, malignant, of male urethra, 390
Metaplasia, adenomatous, of bladder, 453
Metastasis(es)—
  lymph node, of testicular teratoma, response to radiation therapy, 363
  penile, of prostatic carcinoma, regression with cyproterone acetate therapy, 268
  testicular from prostatic carcinoma, 498
  ureteric, contralateral, from renal carcinoma, 402
Micturition, increased frequency, and effect on introital bacterial flora, 211
Multiple sclerosis—
  and abnormalities of detrusor and sphincter function, 193
  bladder and urethral innervation in, 239
  with rupture of a bladder diverticulum, 382
Muscles, smooth and striated, in canine urethral pressure profile, 347

Nephrectomy—
  allograft, 413
  complication of, by supracostal approach, 106
Nephrocalcinosis, diphosphonate therapy, 93
Nephrogenic adenoma, 453
Neuromyopathy, reversible, in hypernephroma, 340
Neuropathic bladder—
  congenital, anti-reflux surgery, 639
  division of external urethral sphincter in, 649
Nitrous oxide, liquid, use in cryosurgery for prostatic obstruction, 203

Obstruction, pseudocyst formation and hypertension in traumatic avulsion of the ureter, 107
Occupational bladder tumour, cases identified, 561
Oligozoospermia, A.I.H. for, 499
Osteolytic lesion as a presentation of bladder carcinoma, 254

Papillomas, inverted, of lower urinary tract, 567
Pelvic hydronephrosis, primary, in children, 549
Pelvis, renal, leukoplakia of, 376
Pelvi-ureteric obstruction, reflux induced, 555
Penile metastases of prostatic carcinoma, regression with cyproterone acetate therapy, 268
Penis—
  amoebiasis of, 269
  filariasis of, 426
  tuberculosis of, 274
Percutaneous suprapubic cystostomy after spinal cord injury, 119
Perfusion of CO_2, to record urethral pressure profile, 337
Peritoneal tuberculosis with ureteric obstruction, mimicking retroperitoneal fibrosis, 170
Pfannenstiel incision, reappraisal of, 469
Phaeochromocytoma—
  of bladder, coexisting with carcinoma, 123
  of urinary bladder, gynaecological presentation, 468
Plasma gonadotrophic hormones, testicular biopsy and seminal analysis in men of infertile marriages, 709
Polycythaemia, and hydronephrosis, 175
Polyp(s)—
  urethral, congenital, in a child, 278
  urethral, congenital posterior, causing urinary retention, 478
Posterior urethral duplication, 264
Posterior urethral valves in siblings, 76
Pressure/flow studies in children with upper urinary tract obstruction, 427
Prostaglandins, and their synthesis inhibitors, action on detrusor muscle, 631
Prostate—
  carcinoma of, latent, 207
  carcinoma of, lymphography and pelvic lymphadenectomy in, 689
  carcinoma of, random bone marrow biopsy in staging of, 265
  concentrations of trimethoprim-sulphamethoxazole in, 77
  hypertrophy of, benign, effect of bromocriptine, 73
Prostatic—
  cancer, serum antibody in, 355
  carcinoma, testicular metastasis from, 498
  hypertrophy, benign, testosterone metabolism, studies of gestonorone caproate and cyproterone acetate, 485
    detrusor and urethral dysfunction in, 493
  obstruction, benign, use of alpha-adrenergic blockers, 255
    cryosurgery for, using liquid nitrous oxide, 203
  resection, hypothermic, 685
    transurethral, prophylactic antibiotics in, 479
  urethral calculi, 492
Prostatism investigated by excretion urography, 681
Prostatitis, chronic bacterial, 245
Proteus stone, surgical significance, 399
Prune belly syndrome, urodynamics in, 663
Pseudocyst formation and hypertension in traumatic avulsion of the ureter, 107
PUIGVERT FOUNDATION, Barcelona. Announcement of the XL Annual International Urological Symposium, 1976, 294
Pyelonephritis, ascending, Ask-Upmark kidney as a form of, 393
Pyonephrosis, renal calculous, causing duodenal and common bile duct obstruction with pyeloduodenal fistula, 6

Radiotherapy—
  in treatment of recurrent bladder cancer, 595
  radical *v.* preoperative radiotherapy and radical cystectomy, in deeply infiltrating bladder carcinoma, 587
Rat bladders, effects of irrigation solutions, 463
RECENT ADVANCES IN SURGICAL UROLOGY. Announcement of courses at the Royal Postgraduate Medical School, London, 1976, 294

- Reflux—
  - vesico-ureteral, influence on response to treatment of urinary tract infections in female children, 111
  - vesico-ureteric, diagnosis with ultrasonography, 431
- Renal—
  - allografts, surgical correction of arterial stenosis in, 221
  - arteries, fibromuscular dysplasia of, autotransplantation of kidney for, 227
  - calculi, size, recurrence rate and follow-up, 525
  - calculous pyonephrosis, causing duodenal and common bile duct obstruction with pyelo-duodenal fistula, 6
  - carcinoma, contralateral ureteric metastasis from, 402
  - carcinomas, bilateral, treated operatively, 118
  - ectopia, crossed, with colic, 171
  - hypertension, unilateral, following major trauma, 362
  - irrigation with stone solvent, postoperative, and recurrence of infected calculi, 531
  - pedicle, avulsion of, due to blunt injury, 12
  - pelvis, leukoplakia of, 376
  - stones, thermogravimetric analysis, 403
  - tuberculosis, and leukoplakia, 377
- Retroperitoneal fibrosis mimicked by peritoneal tuberculosis with ureteric obstruction, 170

- Sarcoma botryoides, vaginal, long survival after, 452
- Seminal analysis, plasma gonadotrophic hormones and testicular biopsy in men of infertile marriages, 709
- Serum antibody in patients with prostatic cancer, 355
- Short Case Reports—
  - Allan, D. M., Recurrent transitional cell carcinoma complicating ileal conduit, 60
  - Bagley, F. H. and Davidson, A. I. Congenital urethral polyp in a child, 278
  - Bentley, P. G. and Higgs, D. R., Peritoneal tuberculosis with ureteric obstruction, mimicking retroperitoneal fibrosis, 170
  - Blath, R. A. and Bucy, J. G., Localised primary amyloidosis of the bladder, 219
  - Boardman, K. P. Duodenal and common bile duct obstruction with a pyelo-duodenal fistula caused by renal calculous pyonephrosis, 6
  - Condon, J. R., Milsted, R. A. V. and Nassim, J. R., Hyperparathyroidism and sodium cellulose phosphate, 316
  - Di Paola, M. and Stockwell, W. S., Appendico-vesical fistula due to an appendix abscess with associated goblet cell carcinoid of the appendix, 436
  - Farkas, A. and Skinner, D. G., Posterior urethral valves in siblings, 76
  - Feggetter, J. G. W., An osteolytic lesion as a presentation of bladder carcinoma, 254
  - Fischelovitch, J. and Avidor, I., Leukoplakia of renal pelvis, 376
  - Fischelovitch, J. and Ben-Bassat, M., Female hypospadias, 72
  - Fraser, D. M., Franks, A. J. and Campbell, I. W., Reversible neuromyopathy in hypernephroma, 340
  - Gallagher, B. L. S. and Hashmat, A. I., Malignant testicular lymphoma in brothers, 210
  - Gupta, S. and Gupta, I. M., Ectopia vesicae complicated by squamous cell carcinoma, 244
  - Hughes, M. A., Arkell, D. G., Dawson-Edwards, P. and Geddes, J. R., Contralateral ureteric metastasis from renal carcinoma, 402
  - Ipiéns Aznar, A. and Martinez-Peñuela V., J. M., Urinary retention due to congenital posterior urethral polyp in a boy, 478
  - Jackaman, F. R., Recurrent spontaneous rupture of the urinary bladder, 54
  - Jameson, R. M., Regression of penile metastases of prostatic carcinoma with cyproterone acetate, therapy, 268
  - Jenkins, D. G. and Gupta, K. G., Complete avulsion of the renal pedicle due to blunt injury to abdomen, 12
  - Kupelian, S. and Robinson, M. R. G., Pelvic lipomatosis presenting as acute ureteric obstruction, 389
  - Ludgate, C. M. and Watson, G. S., Unilateral renal hypertension following major trauma, 362
  - McLoughlin, M., Ureterocalyostomy, 328
  - Mysorekar, V. R., Accessory vas deferens: a case report, 82
  - Narayan, A. S., Kelly, D. G. and Duff, F. A., Tuberculosis of the penis, 274
  - Oosterlinck, W. and Renders, G., A knot in the urethra, 284
  - Osborne, D. and Gingell, J. C., Posterior urethral duplication, 264
  - Prasad, S., Filariasis penis, 426
  - Salem, R. J. and Luck, R. J., Midline ensheathed ureters, 18
  - Sasidharan, K., Babu, A. S., Rao, M. M. and Bhat, H. S., Free supernumerary kidney, 388
  - Schiff, M. and Feldman, R. A., Lymphocele following renal transplantation: an unusual cause of urinary retention, 122
  - Sharma, S. K., Bapna, B. C. and Singh, S. M., Familial profile of transitional cell carcinoma, 442
  - Sharma, S. K., Wadhwa, S. N. and Chabra, J. S., Primary vaginal stone, 336
  - Shimada, K., Katsumi, T. and Fujita, H., Appendiceal granuloma causing bilateral hydronephrosis and macroscopic haematuria, 418
  - Silverton, N. P., Testicular metastasis from prostatic carcinoma, 498
  - Smith, R. B. and Kettlewell, M. G., Rupture of a bladder diverticulum in multiple sclerosis, 382
  - Stuart, A. E. and Magri, J., Long survival after vaginal sarcoma botryoides, 452
  - Terada, Y. and Takayasu, H., Malignant melanoma of the male urethra, 390
  - Vijayan, P., Clark, P. B. and Anderson, C. K., Leukoplakia of the male urethra, 346
  - Vinson, R. K. and Koff, S. A., Obstructing prostatic urethral calculi, 492
  - Way, S. and Young, J. R., Ureteric invasion by endometriosis, 38
  - Weinberg, R. W., Appendix ureteroplasty, 234
  - Wesolowski, S., Bilateral renal carcinomas treated operatively, 118
  - Wesolowski, S., Ileal replacement of ureter of solitary kidney: 22-year follow-up, 292
  - Whyte, A. S. and Dick, A. A gynaecological presentation of phaeochromocytoma of the urinary bladder, 468
  - Williams, G. and Castro, J. E., A complication of nephrectomy by the supracostal approach, 106

Sodium cellulose phosphate and hyperparathyroidism, 316
Sperm antibodies, A.I.H. for, 499
Sphincter—
  artificial implantable, 675
  external urethral, division in neuropathic bladder, 649
  function, abnormalities, in multiple sclerosis, 193
Sphincteric activity following trans-sphincteric urethral reconstruction, 643
Spinal cord injury, vesical outlet obstruction in, surgical treatment, 657
Squamous cell carcinoma, complicating ectopia vesicae, 244
Stenosis, arterial, in renal allografts, surgical correction, 221
Sterile bag—
  clean catch and suprapubic aspiration in diagnosis of urinary infection in early childhood, 279
  comparison with clean catch and suprapubic aspiration in diagnosis of urinary infection in early childhood, 279
STIFTUNG C. E. ALKEN PRIZE: Announcement, 91
Stone(s)—
  bladder, endemic, of Indonesia, 617
  calcium, and uric acid disorders, 1
    management of patient, 507
  Proteus, surgical significance, 399
  renal, thermogravimetric analysis, 403
  vaginal, primary, 336
Supernumerary kidney, free, 388
Suprapubic aspiration, comparison with sterile bag and clean catch in diagnosis of urinary infection in early childhood, 279
SYMPOSIUM ON DIAGNOSTIC ULTRASOUND IN GASTROENTEROLOGY AND UROLOGY, Johns Hopkins Hospital, 1976: Announcement, 294

Television transmission, live, of transurethral and open pelvic surgery, 475
Teratoma, testicular, lymph node metastases of, response to radiation therapy, 363
Testicular—
  arteries, arching over left renal vein, 135
  biopsy, plasma gonadotrophic hormones and seminal analysis in men of infertile marriages, 709
  lymphoma, malignant, in brothers, 210
  metastasis from prostatic carcinoma, 498
  teratoma, lymph node metastases of, response to radiation therapy, 363
Testosterone metabolism in benign prostatic hypertrophy, studies of gestonorone caproate and cyproterone acetate, 485
Thermogravimetric analysis of renal stones, 403
Thiazide treatment in stone formers and crystalluria, 515
Thiotepa, single dose intravesical, as an adjuvant to cystodiathermy in the treatment of transitional cell bladder carcinoma, 55
Transitional cell carcinoma, familial profile, 442
Transurethral prostatic resection, prophylactic antibiotics in, 479
Transurethral surgery, live television transmission, 475
Trigonal cyst in childhood, 323
Trimethoprim-sulphamethoxazole concentrations in human prostate gland, 77
Trypan blue in the study of viability of non-motile sperms in post-vasectomy patients, and chlorhexidine irrigation, 371
Tuberculosis—
  of penis, 274
  peritoneal, with ureteric obstruction, mimicking retroperitoneal fibrosis, 170
  renal, and leukoplakia, 377
Tuberculous lower ureteric stricture, surgical management, 101
Tumour(s)—
  bladder, hyperthermia in treatment of, 603
    occupational, cases identified, 561

Ultrasonography in diagnosis of vesico-ureteric reflux, 431
Ureter(s)—
  avulsion, traumatic, with obstruction, pseudocyst formation and hypertension, 107
  circumcaval, in children, 183
  elastic component of, in children, 13
  ileal, experience with, 19
    replacement of, of solitary kidney, 292
  midline ensheathed, 18
  normal and dilated, in children, elastic component, 13
  re-implantation of, 31
Ureteric—
  invasion by endometriosis, 38
  metastasis, contralateral, from renal carcinoma, 402
  obstruction, acute, as presentation of pelvic lipomatosis, 389
    and peritoneal tuberculosis, mimicking retroperitoneal fibrosis, 170
  stricture, tuberculous, surgical management, 101
Ureterocalyostomy, 328
Ureterolithiasis mimicked by endometriosis, 27
Ureterolithotomy, vaginal, 231
Ureteroplasty, appendix, 234
Urethra—
  knot in, 284
  male, leukoplakia of, 346
    malignant melanoma of, 390
Urethral—
  calculi, prostatic, 492
  closed pressure profile, using gas and simultaneous EMG-recording from the urethra, 341
  duplication, posterior, 264
  dysfunction in prostatic hypertrophy, 493
  innervation in multiple sclerosis, 239
  polyp, congenital, in a child, 278
    congenital posterior, causing urinary retention, 478
  pressure profile, canine, contributions of smooth and striated muscles, 347
    recorded by CO_2-perfusion at high flow rates, 337
  reconstruction, trans-sphincteric, sphincteric activity after, 643
  sphincter, external, division in neuropathic bladder, 649
  stricture, Badenoch's pull-through operation, 83
  valves, posterior, in siblings, 76
Urethropenile deformity, surgical repairs, 127
Urethroplasty in context, 697
Uric acid disorders in patients with calcium stones, 1
Urinary—
  bladder, effects of drugs and anaesthetic agents on, 329
    phaeochromocytoma, gynaecological presentation, 468
    recurrent spontaneous rupture of, 54

Urinary—
  chemiluminescence, chemical nature of, 61
  citrate excretion in stone-formers and normal controls, 7
  incontinence, in children, anterior detrusor tube repair, 671
  infection, comparison of hydrophilic polymer-coated latex, uncoated latex and PVC in-dwelling balloon catheters in the prevention of, 285
    in childhood, sterile bag, clean catch and supra-pubic aspiration in diagnosis, 279
  retention, caused by lymphocele following renal transplantation, 122
    due to congenital posterior urethral polyp, 478
  sphincters, effects of drugs and anaesthetic agents on, 329
  symptoms and total hysterectomy, 437
  tract, function, lower, standardisation of terminology, 39
    infections, in female children, influence of vesico-ureteral reflux on response to treatment, 111
    lower, inverted papillomas of, 567
      obstruction, upper, pressure/flow studies in children, 427
Urodynamic studies in the District General Hospital, 383
Urodynamics in the prune belly syndrome, 663
Urography, excretion, in the investigation of prostatism, 681
UROLOGICAL SOCIETY OF AUSTRALASIA—
  Abstracts of the Proceedings of the 28th Annual General Meeting, Sydney, 1975, 145
  Announcement of Annual Meeting, Perth 1977, 295

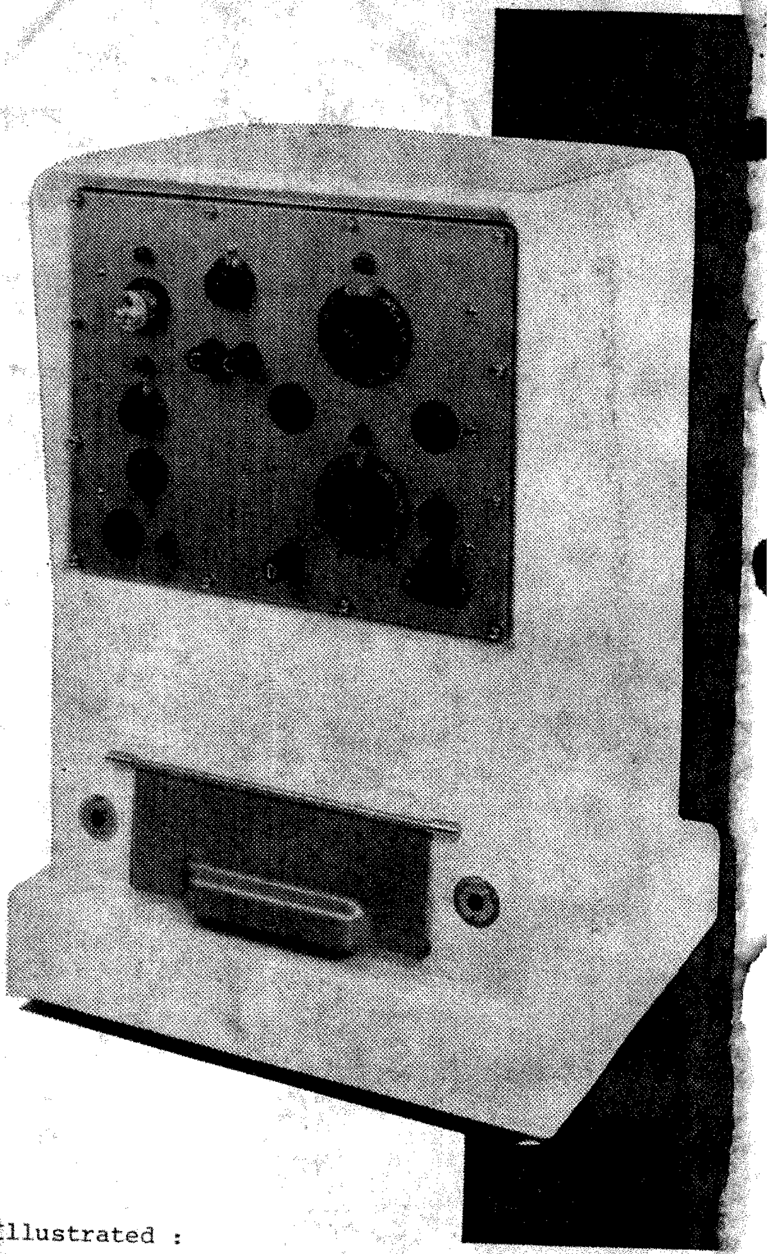
Vaginal sarcoma botryoides, long survival after, 452
Vaginal stone, primary, 336
Vaginal ureterolithotomy, 231
Vas, irrigation with chlorhexidine, 371
Vas deferens, accessory, 82
Vasoplasty, new technique, 275
Vesical outlet obstruction, spinal cord injury, surgical treatment, 657
Vesico-ureteric reflux—
  influence of, on response to treatment of urinary tract infections in female children, 111
    diagnosis with ultrasonography, 431

We know what you want!

AFTER MORE THAN 50 YEARS SERVING THE NEEDS OF UROLOGISTS WE REALISE THAT A RESECTOSCOPE IS ONLY AS GOOD AS THE DIATHERMY MACHINE.

WE KNOW YOU WANT RELIABLE, SAFE, SMOOTH, POWERFUL BUT CONSISTENT CUTTING AND COAGULATING.

WE KNOW YOU WANT EXPERT, FAST SERVICING IN THE EVENT OF A BREAKDOWN.



Illustrated :

Turner-Warwick Urological Unit with spark gap and valve circuits with blender, including fibre light and cautery. GU332A/FLC.

We have what you want

t us send you our new Catalogue
our complete Diathermy range.

GU MFG. CO. LTD.
Plympton St., London, NW.8.

ISSN 000

Printed in Great Britain by T. & A. Constable Ltd, *Hopetoun Street, Edinburgh*